

- 9 -

the aerosol-generating article having a first compartment having a tubular porous element and a second compartment; and an elongate piercing member configured to pierce the first compartment and the second compartment of the aerosol-generating article when an aerosol-generating article is received in the outer housing. The elongate piercing member comprises: a
5 piercing portion adjacent a distal end of the elongate piercing member; a shaft portion; and an obstructing portion adjacent a proximal end of the elongate piercing member. The piercing portion has a maximum diameter greater than the diameter of the shaft portion, and the obstructing portion has an outer diameter such that it fits within the tubular porous element of the first compartment of the aerosol-generating article when an aerosol-generating article is
10 received in the device.

As used herein, the term "aerosol-generating device" refers to an aerosol-generating device that interacts with an aerosol-generating article to generate an aerosol that is directly inhalable into a user's lungs thorough the user's mouth.

According to a yet further aspect of the present invention, there is provided an aerosol-
15 generating article for an aerosol-generating system. The aerosol-generating article comprises: a first compartment having a first end and a second end, comprising a tubular porous element and a delivery enhancing compound including an acid sorbed on the porous tubular element; and a second compartment comprising a volatile liquid including a nicotine formulation having a first end, adjacent the second end of the first compartment, and a second end. The first end of
20 first compartment is sealed by a frangible barrier, the interface between the second end of the first compartment and the first end of the second compartment is sealed by at least one frangible barrier, and the second end of the second compartment is sealed by a frangible barrier.

Preferably each end of each of the first compartment and second compartment is sealed
25 by a frangible barrier. Preferably, the first compartment and the second compartment are formed separately and combined together by abutting the second end of the first compartment with the first end of the second compartment and wrapping both compartments in a wrapper material. The wrapper material may be card or any other suitable material. The wrapper material may extend past the second end of the second compartment to form a mouthpiece or
30 aerosol forming chamber.

The first compartment of the aerosol-generating article preferably comprises a volatile delivery enhancing compound. As used herein, by "volatile" it is meant the delivery enhancing compound has a vapour pressure of at least about 20 Pa. Unless otherwise stated, all vapour pressures referred to herein are vapour pressures at 25°C measured in accordance with
35 ASTM E1194 – 07.

- 10 -

Preferably, the volatile delivery enhancing compound has a vapour pressure of at least about 50 Pa, more preferably at least about 75 Pa, most preferably at least 100 Pa at 25°C.

Preferably, the volatile delivery enhancing compound has a vapour pressure of less than or equal to about 400 Pa, more preferably less than or equal to about 300 Pa, even more preferably less than or equal to about 275 Pa, most preferably less than or equal to about 250 Pa at 25°C.

In certain embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 20 Pa and about 400 Pa, more preferably between about 20 Pa and about 300 Pa, even more preferably between about 20 Pa and about 275 Pa, most preferably between about 20 Pa and about 250 Pa at 25°C.

In other embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 50 Pa and about 400 Pa, more preferably between about 50 Pa and about 300 Pa, even more preferably between about 50 Pa and about 275 Pa, most preferably between about 50 Pa and about 250 Pa at 25°C.

In further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 75 Pa and about 400 Pa, more preferably between about 75 Pa and about 300 Pa, even more preferably between about 75 Pa and about 275 Pa, most preferably between about 75 Pa and about 250 Pa at 25°C.

In yet further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 100 Pa and about 400 Pa, more preferably between about 100 Pa and about 300 Pa, even more preferably between about 100 Pa and about 275 Pa, most preferably between about 100 Pa and about 250 Pa at 25°C.

The volatile delivery enhancing compound may comprise a single compound. Alternatively, the volatile delivery enhancing compound may comprise two or more different compounds.

Where the volatile delivery enhancing compound comprises two or more different compounds, the two or more different compounds in combination have a vapour pressure of at least about 20 Pa at 25°C.

Preferably, the volatile delivery enhancing compound is a volatile liquid.

The volatile delivery enhancing compound may comprise a mixture of two or more different liquid compounds.

The volatile delivery enhancing compound may comprise an aqueous solution of one or more compounds. Alternatively the volatile delivery enhancing compound may comprise a non-aqueous solution of one or more compounds.

- 11 -

The volatile delivery enhancing compound may comprise two or more different volatile compounds. For example, the volatile delivery enhancing compound may comprise a mixture of two or more different volatile liquid compounds.

5 Alternatively, the volatile delivery enhancing compound may one or more non-volatile compounds and one or more volatile compounds. For example, the volatile delivery enhancing compound may comprise a solution of one or more non-volatile compounds in a volatile solvent or a mixture of one or more non-volatile liquid compounds and one or more volatile liquid compounds.

10 The delivery enhancing compound preferably comprises an acid or ammonium chloride. Preferably, the delivery enhancing compound comprises an acid. More preferably, the delivery enhancing compound comprises an acid having a vapour pressure of at least about 5 Pa at 20°C. Preferably, the acid has a greater vapour pressure than nicotine at 20°C.

15 The delivery enhancing compound may comprise an organic acid or an inorganic acid. Preferably, the delivery enhancing compound comprises an organic acid. More preferably, the delivery enhancing compound comprises a carboxylic acid. Most preferably, the delivery enhancing compound comprises an alpha-hydroxy, an alpha-keto or 2-oxo acid.

20 In a preferred embodiment, the delivery enhancing compound comprises an acid selected from the group consisting of lactic acid, 3-methyl-2-oxovaleric acid, pyruvic acid, 2-oxovaleric acid, 4-methyl-2-oxovaleric acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof. In a particularly preferred embodiment, the delivery enhancing compound comprises pyruvic acid.

The tubular porous element is preferably a sorption element with an acid or ammonium chloride sorbed thereon.

25 The tubular porous element may be formed from any suitable material or combination of materials for sorbing a liquid. The tubular porous element may comprise one or more porous materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres. The one or more porous materials may or may not be capillary materials and are preferably inert with respect to the acid or ammonium chloride. The particular preferred porous material or materials will depend on the physical properties of the acid or ammonium chloride. The one or more porous materials may have any suitable porosity so as to be used with different acids having different physical properties. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and BAREX®.

35

- 12 -

Suitable porous fibrous materials include, but are not limited to: cellulose cotton fibres, cellulose acetate fibres and bonded polyolefin fibres, such as a mixture of polypropylene and polyethylene fibres.

5 The size, shape and composition of the tubular porous element may be chosen to allow a desired amount of volatile delivery enhancing compound to be sorbed on the tubular porous element.

In a preferred embodiment, between about 15 μ l and about 200 μ l, more preferably between about 40 μ l and about 150 μ l, most preferably between about 50 μ l and about 100 μ l of the volatile delivery enhancing compound is sorbed on the tubular porous element.

10 The tubular porous element advantageously acts as a reservoir for the delivery enhancing compound.

Preferably, the second compartment comprises a source of nicotine. As such, the volatile liquid within the second compartment preferably comprises one or more of nicotine, nicotine base, a nicotine salt, or a nicotine derivative.

15 The source of nicotine may comprise natural nicotine or synthetic nicotine. The source of nicotine may comprise nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate, or a combination thereof.

20 The source of nicotine may further comprise an electrolyte forming compound. The electrolyte forming compound may be selected from the group consisting of alkali metal hydroxides, alkali metal oxides, alkaline earth metal oxides, sodium hydroxide (NaOH), calcium hydroxide (Ca(OH)₂), potassium hydroxide (KOH) and combinations thereof.

Alternatively or in addition, the source of nicotine may further comprise other components including, but not limited to, natural flavours, artificial flavours and antioxidants.

25 Preferably, the second compartment comprises a liquid nicotine formulation. Preferably, the second compartment is configured to hold between about 5 microlitres and about 50 microlitres of the liquid nicotine formulation, more preferably about 10 microlitres of the liquid nicotine formulation.

The liquid nicotine formulation may comprise pure nicotine, a solution of nicotine in an aqueous or non-aqueous solvent or a liquid tobacco extract.

30 The liquid nicotine solution may comprise an aqueous solution of nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate and an electrolyte forming compound.

35 The second compartment may comprise a sorption element and nicotine sorbed on the sorption element. In a preferred embodiment, the second compartment comprises a volatile liquid nicotine source.

- 13 -

In a preferred embodiment, the aerosol-generating article further comprises an aerosol forming chamber in fluid communication with the first compartment and the second compartment. In use, in a preferred embodiment the nicotine reacts with the acid or ammonium chloride in the gas phase in the aerosol forming chamber to form aerosolised nicotine salt particles.

Alternatively, the delivery enhancing compound vapour may react with the nicotine vapour in the second compartment. In such embodiments the aerosol-generating article may further comprise a third compartment downstream of the second compartment and the delivery enhancing compound vapour may alternatively or in addition react with the nicotine vapour in the third compartment to form an aerosol.

The invention allows a cost effective, compact and easy to use aerosol-generating system to be provided. Furthermore, by using an acid or ammonium chloride as a delivery enhancing agent in aerosol-generating articles according to the invention, the pharmacokinetic rate of the nicotine may be advantageously increased.

It will be understood that the aerosol-generating system may also be regarded as an aerosol delivery system. That is to say, the aerosol-generating system provides means for the volatile liquid, such as a nicotine formulation, and the delivery enhancing compound, such as a pyruvic acid, to mix and generate an aerosol but does not actively generate the aerosol. In the embodiment where the aerosol-generating article comprises a third compartment, the third compartment is preferably downstream of the second compartment. Where the article comprises an aerosol forming chamber, the third compartment is preferably downstream of the aerosol forming chamber. The third compartment may comprise a flavour source. Alternatively or in addition, the third component may comprise a filtration material capable of removing at least a portion of any unreacted acid or ammonium chloride mixed with aerosolised nicotine salt particles drawn through the third compartment. The filtration material may comprise a sorbent, such as activated carbon. As will be appreciated, any number of additional compartments may be provided as desired. For example, the article may comprise a third compartment comprising a filter material and a fourth compartment downstream of the third compartment comprising a flavour source.

As will be appreciated, a number of factors influence the formation of the nicotine salt particles. In general, in order to control the nicotine delivery it is important to control the vapourisation of the nicotine formulation and the acid or ammonium chloride. It is also important to control the relative quantities of the nicotine and the acid or ammonium chloride. In the preferred embodiment, the molar ratio of acid to nicotine in the aerosol forming chamber is about 1:1. The use of acid or ammonium chloride as a delivery enhancing compound has been

found to approximately double the delivery rate of nicotine to a user for equivalent power supplied to the vaporiser.

The vaporisation of the acid or ammonium chloride is controlled by the concentration of the acid or ammonium chloride in the first compartment, and by the exchange surface area of acid or ammonium chloride in the first compartment. The vaporisation of the acid or ammonium chloride may be controlled by heating the first compartment of the aerosol-generating article or by heating ambient air drawn through the device before it passes through the first compartment of the aerosol-generating article. In preferred embodiments where the first compartment comprises pyruvic acid, preferably about 60 micrograms of pyruvic acid is vaporised per puff.

Providing an obstructing portion enables the quantity of delivery enhancing compound vaporised per puff to be increased as compared to an aerosol-generating system without such an obstructing portion.

Preferably, the article comprises an opaque outer housing. This advantageously reduces the risk of degradation of the acid or ammonium chloride and nicotine formulation due to exposure to light.

Preferably, the cartridge is not refillable. Thus, when the nicotine formulation in the second compartment of the aerosol-generating article has been used up, the aerosol-generating article is replaced.

In certain embodiments, the device as well as the aerosol-generating article may be disposable.

Advantageously, all elements of the device which are potentially in contact with the acid or ammonium chloride or the source of nicotine are changed when the aerosol-generating article is replaced. This avoids any cross-contamination in the device between different mouthpieces and different aerosol-generating articles, for example aerosol-generating articles comprising different acids or sources of nicotine.

The nicotine formulation in the second compartment may be advantageously protected from exposure to oxygen (because oxygen cannot generally pass through the barrier of the second compartment until it is pierced by the piercing member) and in some embodiments light, so that the risk of degradation of the nicotine formulation is significantly reduced. Therefore, a high level of hygiene can be maintained.

The aerosol-generating article is preferably substantially cylindrical in shape. The aerosol-generating article may have a transverse cross-section of any suitable shape. Preferably, the aerosol-generating article is of substantially circular transverse cross-section or of substantially elliptical transverse cross-section. More preferably, the aerosol-generating article is of substantially circular transverse cross-section.

- 15 -

Preferably, the aerosol generating article has a transverse cross-section substantially the same shape as the cavity of the aerosol-generating device.

A housing of the aerosol-generating article may simulate the shape and dimensions of a tobacco smoking article, such as a cigarette, a cigar, a cigarillo or a pipe, or a cigarette pack. In a preferred embodiment, the housing simulates the shape and dimensions of a cigarette.

The aerosol-generating device and aerosol-generating article may be arranged to releasably lock together when engaged.

The outer housing of the device may be formed from any suitable material or combination of materials. Examples of suitable materials include, but are not limited to, metals, alloys, plastics or composite materials containing one or more of those materials. Preferably, the outer housing is light and non-brittle.

The aerosol-generating system and device are preferably portable. The aerosol-generating system may have a size and shape comparable to a conventional smoking article, such as a cigar or cigarette.

Any feature in one aspect of the invention may be applied to other aspects of the invention, in any appropriate combination. In particular, method aspects may be applied to apparatus aspects, and vice versa. Furthermore, any, some and/or all features in one aspect can be applied to any, some and/or all features in any other aspect, in any appropriate combination.

It should also be appreciated that particular combinations of the various features described and defined in any aspects of the invention can be implemented and/or supplied and/or used independently.

The invention will be further described, by way of example only, with reference to the accompanying drawings in which:

Figures 1(a) and 1(b) show a schematic representation of aerosol-generating systems according to the present invention;

Figures 2 show an aerosol-generating article according to the present invention being inserted into an aerosol-generating device according to the present invention;

Figure 3 shows the air flow pathway through the aerosol-generating system of Figure 1;

Figure 4 shows a graph of test data showing the improved nicotine delivery for an aerosol-generating system having an obstructing portion which acts as a flow restrictor; and

Figure 5 shows an alternative embodiment of an aerosol-generating system according to the present invention.

Figure 1(a) shows a schematic representation of an aerosol-generating system 100. The system 100 comprises an aerosol-generating device 102 and an aerosol-generating article 104.

- 16 -

The aerosol-generating article 104 has an elongate cylindrical shape and comprises a first compartment 106 comprising a volatile delivery enhancing compound source, and a second compartment 108 comprising a volatile liquid nicotine source. The first compartment 106 and the second compartment 108 are arranged in series and abut each other in axial alignment.

5 The first compartment 106 is positioned at the distal, or upstream, end of the aerosol-generating article 104. The second compartment 108 is positioned downstream of the first compartment. A further element (not shown) in the form of a mouthpiece or the like may be provided at the downstream end of the second compartment.

10 The upstream and downstream ends of the first compartment 106 and the second compartment 108 of the aerosol-generating article 104 are sealed by frangible barriers 110, 112 and 114, 116 respectively. The frangible barriers are made from metal film, such as aluminium.

The aerosol-generating device 102 comprises an outer housing 118 having an elongate cylindrical cavity configured to receive the aerosol-generating article 104. The longitudinal length of the cavity is less than the length of the article 104 such that the proximal, or

15 downstream, end of the article 104 protrudes from the cavity.

The device 102 further comprises an elongate piercing member 120. The piercing member is positioned centrally within the cavity of the aerosol-generating device and extends along the longitudinal axis of the cavity. At the proximal end the piercing member 120 comprises a piercing portion 122 in the form of a cone having a circular base. At the distal end

20 the piercing member further comprises an obstructing portion 124 which, in use, acts as a flow restrictor and forms a desired air flow pathway. The piercing portion 122 and the obstructing portion 124 are mounted on a shaft 126.

Air inlets (not shown) are provided at the distal, upstream, end of the aerosol-generating device 102. Air outlets (not shown) are provided at the proximal, downstream, end of the

25 aerosol-generating article 104.

Figure 1(b) shows a similar aerosol-generating system 128 as that shown in Figure 1(a), and like numerals have been used to reference similar components. As can be seen, the diameter of the obstructing portion 130 is such that it fits within the tubular porous element 106 to act as a flow restrictor to form a desired air flow pathway as described herein.

30 Figures 2(a) to (e) show the article 104 being inserted into the device 102. Figure 2(a) shows the piercing member 120 engaging with the article 104. The piercing portion 122 breaks the frangible barrier 110 and creates a hole in the barrier having a diameter approximately equal to the maximum diameter of the piercing portion. The maximum diameter of the piercing portion is the diameter of the base circle of the cone which forms the piercing portion. As can be seen

- 17 -

the internal diameter of the device cavity relative to the external diameter of the article 104 is such that the article is located centrally within the cavity.

Figure 2(b) shows the piercing portion engaging with the second frangible barrier of the first compartment 106. Again, the piercing portion breaks the frangible barrier 112 and creates a hole in the barrier having a diameter approximately equal to the maximum diameter of the piercing portion. As can be seen, the maximum diameter of the piercing portion is approximately equal to the internal diameter of the tubular porous element 106. At this stage, the piercing portion also breaks through the first frangible barrier 114 of the second compartment 108, and creates a hole in the barrier having a diameter approximately equal to the maximum diameter of the piercing portion.

Figure 2(c) shows the piercing engaging with the second frangible barrier of the second compartment. Again, the piercing portion breaks the frangible barrier 116 and creates a hole in the barrier having a diameter approximately equal to the maximum diameter of the piercing portion.

Figure 2(d) shows the obstructing, flow restrictor, portion 124 engaging with the tubular porous element 106. As can be seen, the external diameter of the obstructing, flow restrictor, portion is larger than the internal diameter of the tubular porous element such that it forms an interference fit in the tubular porous element. The main function of the interference fit is to define the air flow pathway, as described in further detail below, but the interference fit may also aid in the retention of the article within the device during use.

Figure 2(e) shows the article 104 fully inserted into the device, ready for use. As can be seen, the obstructing, flow restrictor, portion is positioned centrally within the tubular porous element 106, and the piercing portion 122 extends past the proximal, downstream, end of the second compartment.

As shown in Figure 3, in use, when the aerosol-generating article 104 is fully inserted into the aerosol-generating device 102, an air flow pathway, shown by the arrows 200, is formed through the aerosol-generating system. The air flow pathway extends from the distal, upstream end of the aerosol-generating article 104 through the air inlets to the proximal, downstream, end of the article 104. The obstructing, flow restrictor, portion 124 ensures that the air flow pathway extends through the tubular porous element 106.

In use, and as described above, as the aerosol-generating article 104 is inserted into the cavity of the aerosol-generating device 102 the piercing member 120 is inserted into the aerosol-generating article 104 and pierces the frangible barriers 110, 112, 114 and 116 at the upstream and downstream ends of the first compartment 106 and second compartment 108 of the aerosol-generating article 104. This allows a user to draw air into the aerosol-generating

- 18 -

article through the air inlets at the distal, upstream, end thereof, downstream through the tubular porous element 106, and the second compartment 108 and out of the article through the air outlets at the proximal, downstream, end thereof. The obstructing, flow restrictor, portion 124 ensures that the air flow pathway extends through the porous material of the tubular porous element 106. The air flow pathway extends about the shaft of the piercing member via the hole made in the frangible barriers 112, and 114 by the piercing portion 122. The air flow pathway further extends about the shaft of the piercing member via the hole made in the frangible barrier 116 at the proximal, downstream end of the second compartment, and then about the piercing portion 122. By providing a shaft having a smaller diameter than the maximum diameter of the piercing portion, the air flow pathway is enabled to extend around the shaft in the region of the frangible barrier.

Delivery enhancing compound vapour, which in the preferred embodiment contains pyruvic acid, is released from the delivery enhancing compound sorbed on the tubular porous element 106 into the air stream drawn through the aerosol-generating article 104 and nicotine vapour is released from the volatile liquid nicotine source in the second compartment 108 into the air stream drawn through the aerosol-generating article 104. The delivery enhancing compound vapour reacts with the nicotine vapour in the gas phase in the second compartment 108 to form an aerosol, which is delivered to the user through the proximal, downstream, end of the aerosol-generating article 104.

Figure 4 shows experimental data which compares the nicotine delivery per five puffs of the aerosol-generating system with and without the obstructing, flow restrictor, portion on the piercing member. As can be seen, inclusion of the obstructing, flow restrictor, portion increases the overall mass of nicotine delivered over the total of 15 puffs by over 100%.

Figure 5 shows a schematic representation of an aerosol-generating system 500. The system 500 comprises an aerosol-generating device 102, which is the same as that described above in relation to Figures 1 to 3, and an aerosol-generating article 502. The aerosol-generating article 502 has an elongate cylindrical shape and comprises a first compartment 504 comprising a delivery enhancing compound source, and a second compartment 506 comprising a volatile liquid nicotine source. The first compartment 504 and the second compartment 506 are arranged in series and are in axial alignment. The first compartment 504 and the second compartment 506 each comprise a tubular porous element for sorbing the respective liquids stored therein.

The first compartment 504 is positioned at the proximal, or downstream, end of the aerosol-generating article 502. The second compartment 506 is positioned upstream of the first compartment. As will be appreciated, the order of the compartments in this embodiment is

- 19 -

opposite to the order of the compartments in the embodiment described in relation to Figures 1 to 3. Again, a further element (not shown) in the form of a mouthpiece or the like may be provided at the downstream end of the second compartment.

5 The upstream and downstream ends of the first compartment 504 and the second compartment 506 of the aerosol-generating article 502 are sealed by frangible barriers 508, 510 and 512, 514 respectively. The frangible barriers are made from metal film, such as aluminium.

Air outlets (not shown) are provided at the proximal, downstream, end of the aerosol-generating article 502.

10 In this embodiment, the obstructing portion 124, fits in the tubular porous portion of the second compartment 506, and ensures that the airflow pathway 516 extends through the tubular porous element of the second compartment 506. The airflow entrains nicotine, which in turn passes through the first compartment 504 comprising the delivery enhancing compound. The delivery enhancing compound reacts with the nicotine vapour in the gas phase in the first compartment 504 to form an aerosol, which is delivered to the user through the proximal,
15 downstream, end of the aerosol-generating article 502.

The invention has been exemplified above by reference to aerosol-generating systems comprising aerosol-generating devices comprising a piercing member having a conical piercing portion. However, it will be appreciated that aerosol-generating systems and aerosol-generating devices according to the invention may comprise other forms of piercing portion.

20

- 20 -

CLAIMS:

1. An aerosol-generating system comprising:
an aerosol-generating device in cooperation with an aerosol-generating article;
5 the aerosol-generating article comprising:
a first sealed compartment comprising a tubular porous element and a delivery
enhancing compound sorbed on the tubular porous element; and
a second compartment comprising a volatile liquid,
the aerosol-generating device comprising:
10 an outer housing adapted to receive the aerosol-generating article;
an elongate piercing member for piercing the first compartment and the second
compartment of the aerosol-generating article,
wherein, the elongate piercing member comprises:
a piercing portion adjacent a distal end of the elongate piercing member;
15 a shaft portion; and
an obstructing portion adjacent a proximal end of the elongate piercing
member;
wherein, the piercing portion has a maximum diameter greater than the
diameter of the shaft portion, and the obstructing portion has an outer diameter
20 such that it fits within the tubular porous element of the article when the aerosol-
generating article is received in the aerosol-generating device.
2. An aerosol-generating system according to Claim 1, further comprising at least one air
inlet upstream of the first compartment and at least one air outlet downstream of the second
25 compartment, the at least one air inlet and the at least one air outlet being arranged to define an
air flow pathway extending from the at least one air inlet to the at least one air outlet via the
tubular porous element of the first compartment around the obstructing portion, and via the
second compartment around the shaft portion.
- 30 3. An aerosol-generating system according to Claim 1, wherein the second compartment
comprises a tubular porous element, the system further comprising at least one air inlet
upstream of the second compartment and at least one air outlet downstream of the first
compartment, the at least one air inlet and the at least one air outlet being arranged to define
an air flow pathway extending from the at least one air inlet to the at least one air outlet via the

- 21 -

tubular porous element of the second compartment around the obstructing portion, and via the first compartment around the shaft portion.

4. An aerosol-generating system according to Claim 1, 2 or 3, wherein the obstructing portion has a diameter such that it forms an interference fit within the tubular porous element.

5. An aerosol-generating system according to any of claims 1 to 4, wherein the obstructing portion has a longitudinal length of between about 25% and about 75% of the longitudinal length of the tubular porous element.

6. An aerosol-generating system according to any of the preceding claims, wherein the tubular porous element is a hollow cylinder.

7. An aerosol-generating system according to Claim 5, wherein the maximum diameter of the piercing portion has a maximum diameter of between about 75% and about 100% of the internal diameter of the hollow cylinder.

8. An aerosol-generating system according to any of the preceding claims when dependent on Claim 1 or 2, wherein the second compartment is a hollow cylinder, and the piercing portion has a maximum diameter of between about 50% and about 75% of the internal diameter of the second compartment.

9. An aerosol-generating system according to any of the preceding claims, wherein the longitudinal length of the elongate piercing member is greater than the total longitudinal length of the first compartment and the second compartment.

10. An aerosol-generating system according to any of the preceding claims, wherein the piercing portion is conical.

11. An aerosol-generating system according to any of the preceding claims, wherein the article further comprises at least one further element.

12. An aerosol-generating system according to Claim 10, wherein the at least one further element comprises a mouthpiece.

- 22 -

13. An aerosol-generating system according to any of the preceding claims, wherein a first end of the first compartment is sealed by a frangible barrier, an interface between a second end of the first compartment and a first end of the second compartment is sealed by at least one frangible barrier, and a second end of the second compartment is sealed by a frangible barrier.

5

14. An aerosol-generating system according to Claim 12, wherein each frangible barrier is made from metal film.

15. An aerosol generating device for use in an aerosol-generating system, comprising:

10 an outer housing adapted to receive an aerosol generating article, the article having a first sealed compartment having a tubular porous element and a second compartment;

an elongate piercing member configured to pierce the first compartment and the second compartment of the article when an article is received in the outer housing,

15 wherein, the elongate piercing member comprises:

a piercing portion adjacent a distal end of the elongate piercing member;

a shaft portion; and

an obstructing portion adjacent a proximal end of the elongate piercing member;

20 wherein, the piercing portion has a maximum diameter greater than the diameter of the shaft portion, and the obstructing portion has an outer diameter such that it fits within the tubular porous element of the article when an article is received in the device.

25 16. An aerosol-generating article for an aerosol-generating system, comprising:

a first sealed compartment having a first end and a second end, comprising a tubular porous element and a delivery enhancing compound including an acid sorbed of the tubular porous element; and

30 a second sealed compartment having a first end, adjacent the second end of the first compartment, and a second end, comprising a volatile liquid including a nicotine formulation,

35 wherein, the first end of first compartment is sealed by a frangible barrier, the interface between the second end of the first compartment and the first end of the second compartment is sealed by at least one frangible barrier, and the second end of the second compartment is sealed by a frangible barrier.

Figure 1(a)

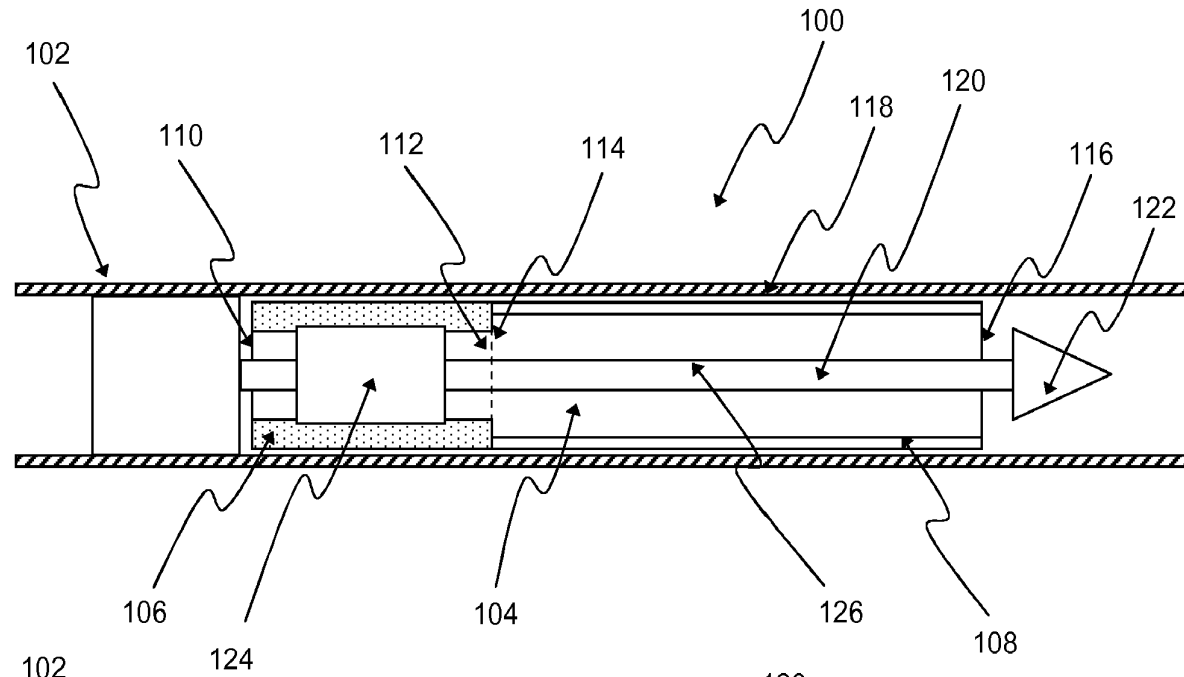
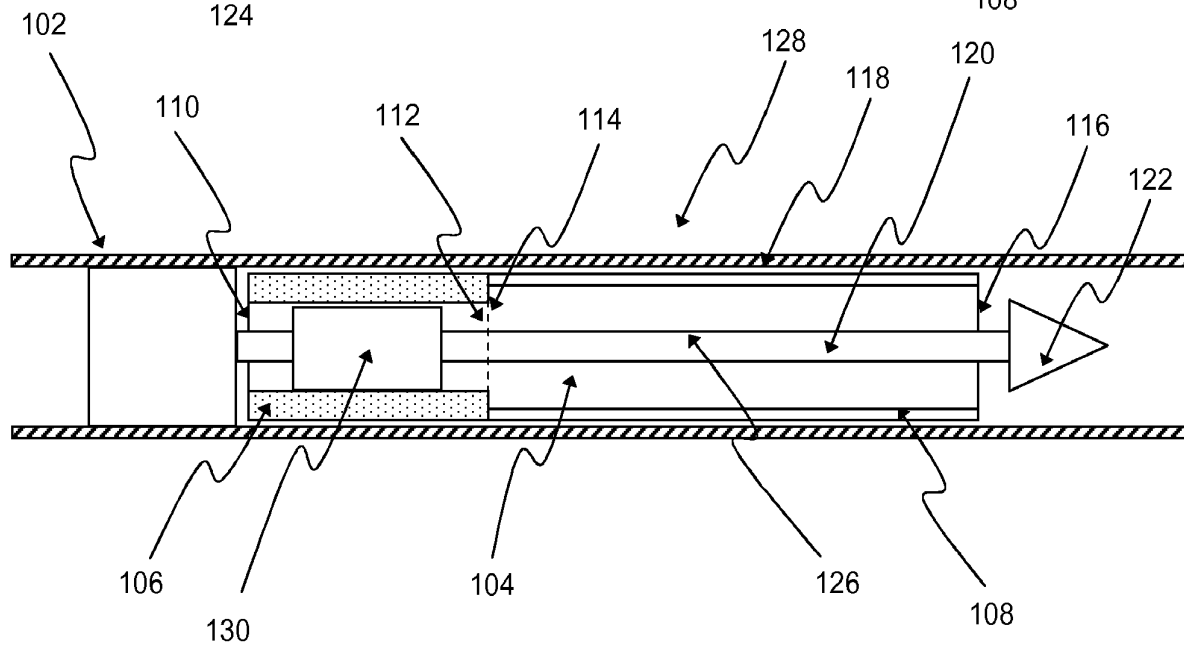


Figure 1(b)



2/5

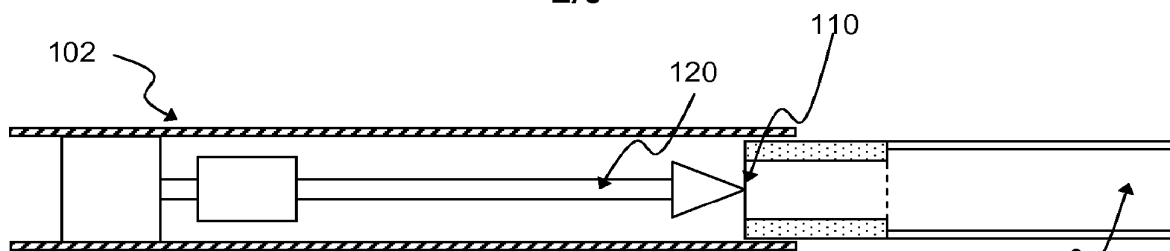


Figure 2(a)

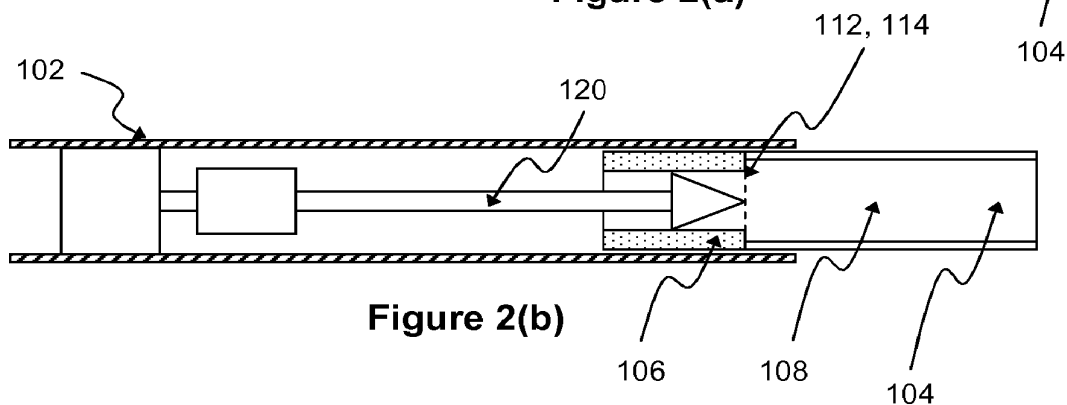


Figure 2(b)

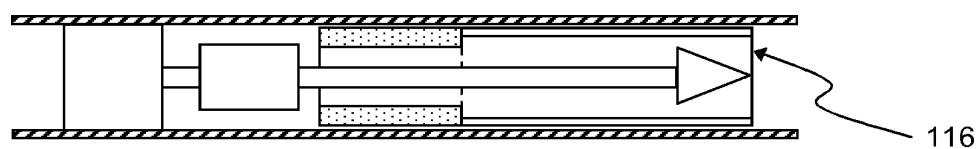


Figure 2(c)

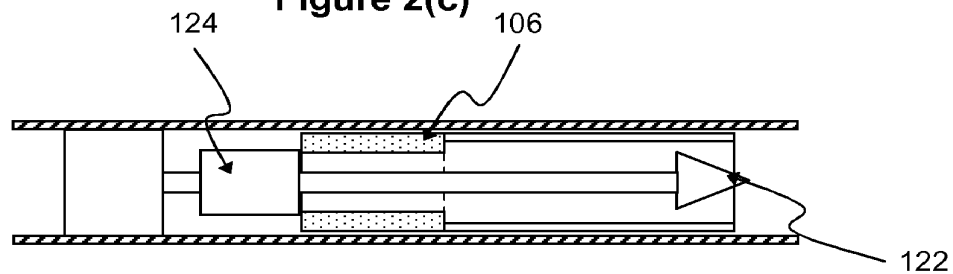


Figure 2(d)

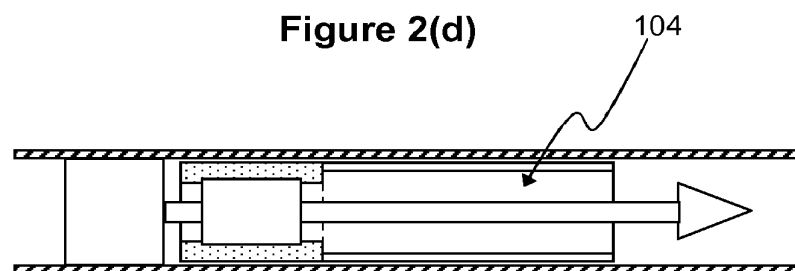
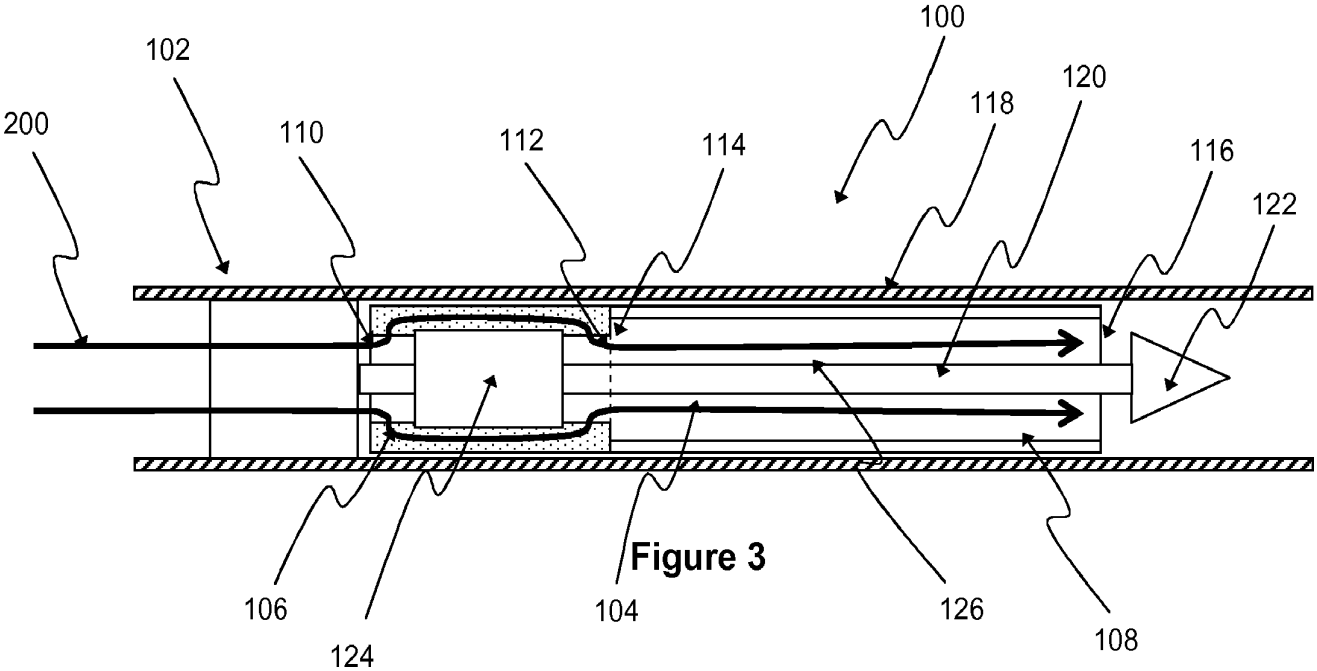
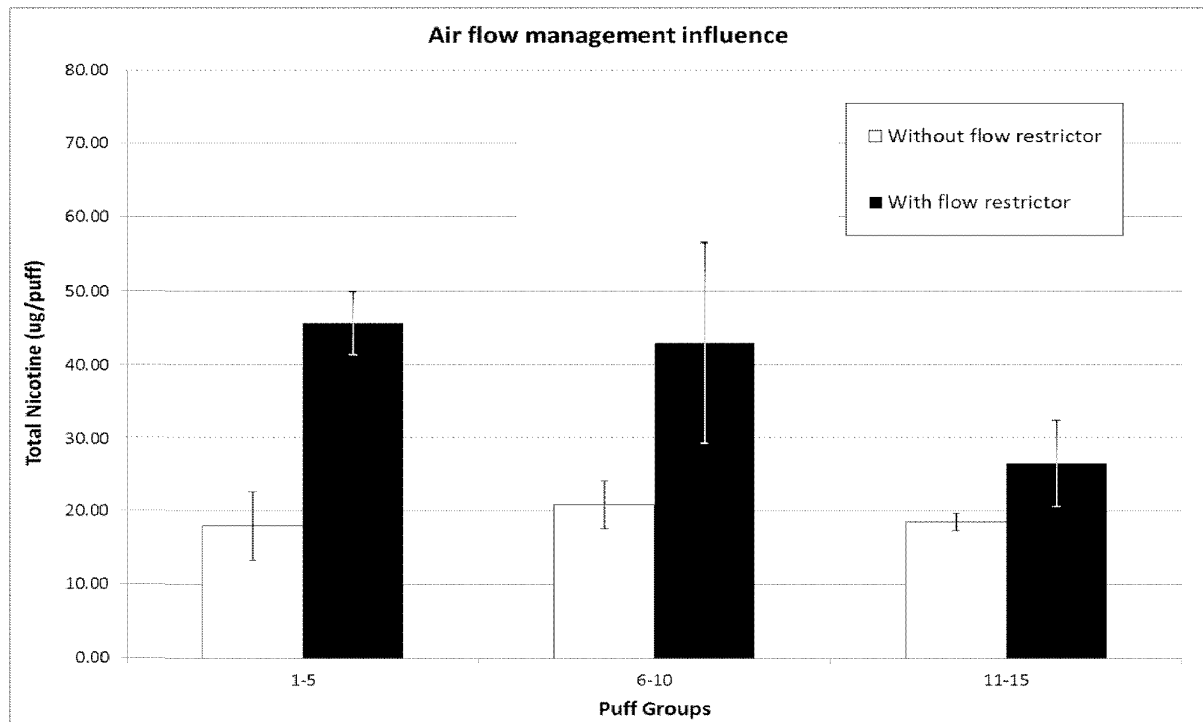
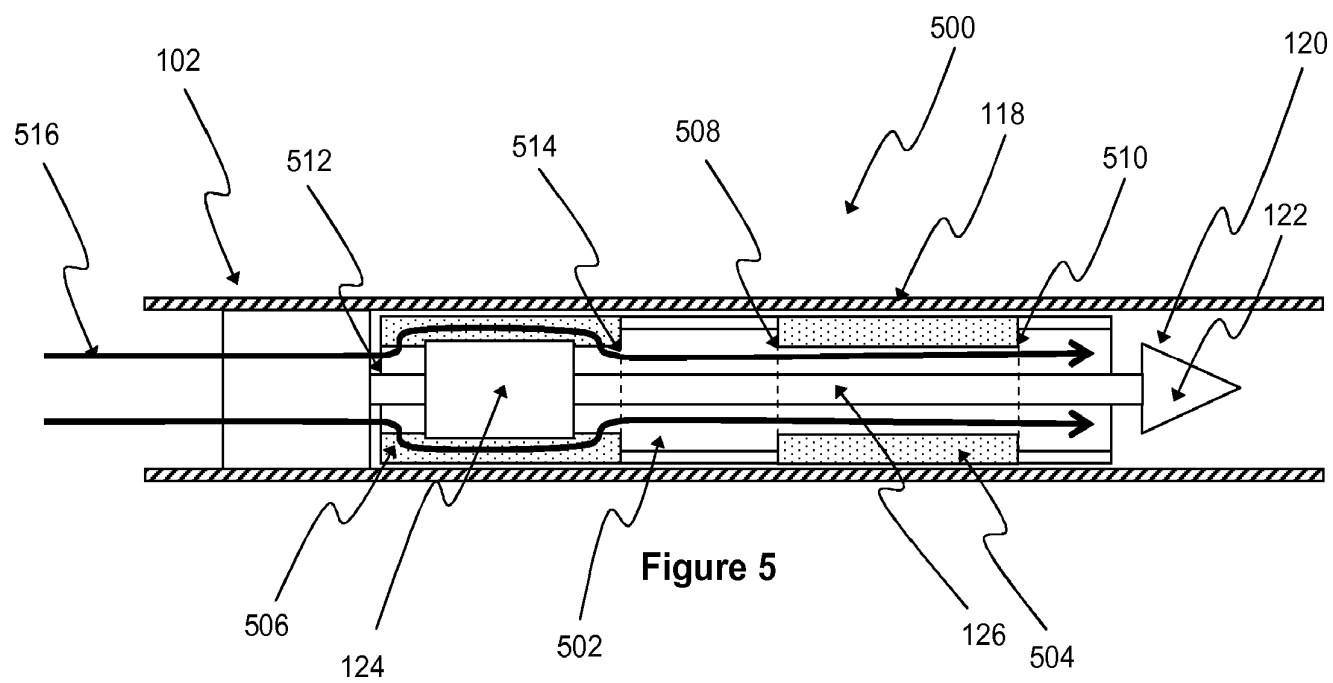


Figure 2(e)



**Figure 4**



INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/054821

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24F47/00 A61M15/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	GB 2 469 850 A (BRITISH AMERICAN TOBACCO CO [GB]) 3 November 2010 (2010-11-03) page 1, lines 3-23 page 5, line 2 - page 6, line 20 figures 5,6 -----	1-15
A	GB 2 473 264 A (BRITISH AMERICAN TOBACCO CO [GB]) 9 March 2011 (2011-03-09) abstract; figures -----	1-15
A	US 4 338 931 A (CAVAZZA CLAUDIO) 13 July 1982 (1982-07-13) abstract; figures 6-8 -----	1-15
A	EP 2 520 186 A1 (SHIMIZU KAZUHIKO [JP]) 7 November 2012 (2012-11-07) abstract; figures 4,5 -----	1-15
	-/--	



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

9 July 2014

Date of mailing of the international search report

16/07/2014

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Kock, Søren

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/054821

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2010/186738 A1 (KOBAYASHI MASAYA [JP] ET AL) 29 July 2010 (2010-07-29) paragraphs [0033] - [0047]; figures 3a,3b34a,4b -----	16
A	EP 1 867 357 A1 (TRENDTECH AS [DK]) 19 December 2007 (2007-12-19) paragraphs [0031] - [0038]; figures -----	16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/054821

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-16

Aerosol generating system and device. A piercing member is provided, the piercing member being provided with a piercing, distal end, an intermediate shaft portion and an obstructing portion at a proximal end. The obstructing portion serves to guide the airflow.

1.1. claim: 16

A multi-compartment article for an aerosol-generating system. The multi-compartment article is provided with sealed compartments whereby the interface between a first and a second compartment is sealed by at least one frangible barrier.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/054821

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 2469850	A	03-11-2010	NONE	
GB 2473264	A	09-03-2011	NONE	
US 4338931	A	13-07-1982	DE 3016127 A1	20-11-1980
			ES 8102816 A1	16-05-1981
			FR 2454813 A1	21-11-1980
			GB 2048689 A	17-12-1980
			IT 1116047 B	10-02-1986
			JP S5615759 A	16-02-1981
			US 4338931 A	13-07-1982
EP 2520186	A1	07-11-2012	EP 2520186 A1	07-11-2012
			JP 4753395 B2	24-08-2011
			JP 2011115141 A	16-06-2011
			US 2012234821 A1	20-09-2012
			WO 2011068020 A1	09-06-2011
US 2010186738	A1	29-07-2010	EP 2173422 A1	14-04-2010
			JP 5137710 B2	06-02-2013
			JP 2009045441 A	05-03-2009
			US 2010186738 A1	29-07-2010
EP 1867357	A1	19-12-2007	AR 061436 A1	27-08-2008
			EP 1867357 A1	19-12-2007
			WO 2007143993 A2	21-12-2007

(10) International Publication Number
WO 2014/187763 A1(43) International Publication Date
27 November 2014 (27.11.2014)

(51) International Patent Classification:

A61M 11/00 (2006.01) A61M 15/06 (2006.01)
A61M 15/00 (2006.01) A24F 47/00 (2006.01)

(21) International Application Number:

PCT/EP2014/060204

(22) International Filing Date:

19 May 2014 (19.05.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

13168613.1 21 May 2013 (21.05.2013) EP

(71) Applicant: **PHILIP MORRIS PRODUCTS S.A.**
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).(72) Inventor: **MALGAT, Alexandre**; Rue des Oiseaux 4F,
CH-1422 Les Tuileries de Grandson (CH).(74) Agent: **MILLBURN, Julie**; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: AEROSOL COMPRISING DISTRIBUTING AGENT AND A MEDICAMENT SOURCE

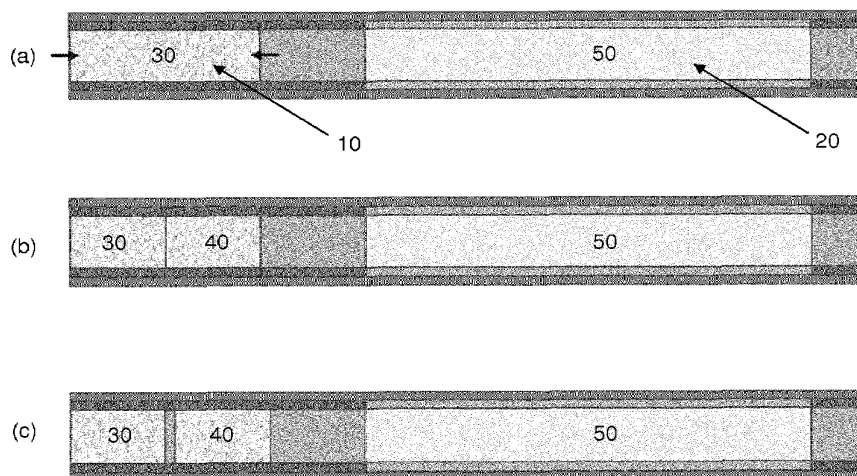


Figure 1

(57) Abstract: An aerosol-generating system comprises a medicament source (20) and a volatile delivery enhancing compound source (10). The volatile delivery enhancing compound source (10) comprises a first sorption element (30), a second sorption element (40) downstream of the first sorption element (30) and a volatile delivery enhancing compound sorbed on the first sorption element (30) and the second sorption element (40), wherein the rate of release of the volatile delivery enhancing compound from the first sorption element (30) is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element (40).

AEROSOL COMPRISING DISTRIBUTING AGENT AND A MEDICAMENT SOURCE

The present invention relates to an aerosol-generating system and an aerosol-generating article for use in an aerosol-generating system. In particular, the present invention relates to an aerosol-generating system for generating an aerosol comprising nicotine salt particles and an aerosol-generating article for use in such an aerosol-generating system.

WO 2008/121610 A1, WO 2010/107613 A1 and WO 2011/034723 A1 disclose devices for delivering nicotine or other medicaments to a user comprising a volatile acid, such as pyruvic acid, or other volatile delivery enhancing compound source and a nicotine or other medicament source. The volatile delivery enhancing compound is reacted with nicotine in the gas phase to form an aerosol of nicotine salt particles that is inhaled by the user.

Figs. 2A-2C of WO 2010/107613 A1 show an exemplary device having a sequential configuration, which is used in Experiment #8 of WO 2010/107613 A1. As shown in Figs. 2A-2C and described in paragraph [0052] and Experiment #8 of WO 2010/107613 A1, this experimental device comprises a tobacco source element 20 (moistened tobacco moisture packed in between rolled stainless steel screen and Teflon outer housing) and a pyruvic acid source element 30 (pyruvic acid in air-freshener plug) separated by a gap 60.

It would be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1, WO 2010/107613 A1 and WO 2011/034723 A1 in which the delivery of nicotine salt particles to a user is improved. It would be especially desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1, WO 2010/107613 A1 and WO 2011/034723 A1 in which the consistency of nicotine salt particle delivery to a user is improved.

It would also be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1, WO 2010/107613 A1 and WO 2011/034723 A1 that allows for improved control of the delivery of nicotine salt particles to a user.

According to the invention there is provided an aerosol-generating system comprising: a medicament source; and a volatile delivery enhancing compound source, the volatile delivery enhancing compound source comprising: a first sorption element; a second sorption element downstream of the first sorption element; and a volatile delivery enhancing compound sorbed on the first sorption element and the second sorption element, wherein the rate of release of the volatile delivery enhancing compound from the first sorption element is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element.

According to the invention there is also provided an aerosol-generating system comprising: an aerosol-generating article, the aerosol-generating article comprising: a medicament source; and a volatile delivery enhancing compound source, the volatile delivery

enhancing compound source comprising: a first sorption element; a second sorption element downstream of the first sorption element; and a volatile delivery enhancing compound sorbed on the first sorption element and the second sorption element, wherein the rate of release of the volatile delivery enhancing compound from the first sorption element is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element.

According to the invention there is further provided an aerosol-generating system comprising: an aerosol-generating article comprising: a medicament source; and a volatile delivery enhancing compound source, the volatile delivery enhancing compound source comprising: a first sorption element; a second sorption element downstream of the first sorption element; and a volatile delivery enhancing compound sorbed on the first sorption element and the second sorption element, wherein the rate of release of the volatile delivery enhancing compound from the first sorption element is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element; and an aerosol-generating device in cooperation with the aerosol-generating article, the aerosol generating device comprising heating means for heating one or both of the medicament source and the volatile delivery enhancing compound source of the aerosol-generating article.

According to the invention there is further provided an aerosol-generating article for use in an aerosol-generating system according to the invention, the aerosol-generating article comprising: a medicament source; and a volatile delivery enhancing compound source, the volatile delivery enhancing compound source comprising: a first sorption element; a second sorption element downstream of the first sorption element; and a volatile delivery enhancing compound sorbed on the first sorption element and the second sorption element, wherein the rate of release of the volatile delivery enhancing compound from the first sorption element is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element.

As used herein, the term "volatile" refers to a delivery enhancing compound having a vapour pressure of at least about 20 Pa. Unless otherwise stated, all vapour pressures referred to herein are vapour pressures at 25°C measured in accordance with ASTM E1194 – 07.

As used herein, by "sorbed" it is meant that the delivery enhancing compound is adsorbed on the surface of the sorption element, or absorbed in the sorption element, or both adsorbed on and absorbed in the sorption element.

As used herein, the term "aerosol-generating device" refers to a device that interacts with an aerosol-generating article to generate an aerosol that is directly inhalable into a user's lungs thorough the user's mouth.

As used herein, the terms "upstream", "downstream", "proximal" and "distal" are used to describe the relative positions of components, or portions of components, of aerosol-generating articles and aerosol-generating systems according to the invention.

The aerosol-generating article or system comprises a proximal end through which, in use, an aerosol exits the aerosol-generating article or system. The proximal end may also be referred to as the mouth end. In use, a user draws on the proximal or mouth end of the aerosol-generating article or system in order to inhale an aerosol generated by the aerosol-generating article or system. The aerosol-generating article or system comprises a distal end opposed to the proximal or mouth end. The proximal or mouth end of the aerosol-generating article or system may also be referred to as the downstream end and the distal end of the aerosol-generating article or system may also be referred to as the upstream end. Components, or portions of components, of the aerosol-generating article or system may be described as being upstream or downstream of one another based on their relative positions between the proximal or downstream end and the distal or upstream end of the aerosol-generating article or system.

The upstream and downstream ends of the aerosol-generating article are defined with respect to the airflow when a user draws on the proximal or mouth end of the aerosol-generating article. Air is drawn into the aerosol-generating article at the distal or upstream end, passes downstream through the aerosol-generating article and exits the aerosol-generating article at the proximal or downstream end.

As used herein, the term "longitudinal" is used to describe the direction between the downstream or proximal end and the opposed upstream or distal end and the term "transverse" is used to describe the direction perpendicular to the longitudinal direction.

The rate of release of the delivery enhancing compound from the first sorption element of the delivery enhancing compound source of aerosol-generating systems according to the invention at a given temperature is greater than the rate of release of the delivery enhancing compound from the second sorption element of the delivery enhancing compound source of aerosol-generating systems according to the invention. As described further below, in use the inclusion of a delivery enhancing compound source comprising a first sorption element and a second sorption element that release the delivery enhancing compound at different rates advantageously improves the delivery of the medicament to a user. In particular, the inclusion of a delivery enhancing compound source comprising a first sorption element and a second sorption element that release the delivery enhancing compound at different rates advantageously improves the consistency of the medicament delivery to a user.

The inclusion in aerosol-generating systems according to the invention of a delivery enhancing compound source comprising a first sorption element and a second sorption element that release the delivery enhancing compound at different rates also advantageously allows for improved control of the delivery of the medicament to a user.

Preferably, the rate of release of the delivery enhancing compound from the first sorption element is at least two times the rate of release of the delivery enhancing compound from the second sorption element. More preferably, the rate of release of the delivery enhancing

compound from the first sorption element is at least three times the rate of release of the delivery enhancing compound from the second sorption element.

In certain embodiments, the rate of release of the delivery enhancing compound from the first sorption element may be between about two times and about ten times the rate of release of the delivery enhancing compound from the second sorption element. In other embodiments, the rate of release the rate of release of the delivery enhancing compound from the first sorption element may be between about three times and about ten times the rate of release of the delivery enhancing compound from the second sorption element.

The air permeability of the first sorption element may be greater than the air permeability of the second sorption element. In such embodiments the increased air permeability of the first sorption element relative to the second sorption element may increase the rate of release of the delivery enhancing compound from the first sorption element relative to the rate of release of the delivery enhancing compound from the second sorption element.

Preferably, the air permeability of the first sorption element as measured in accordance with ISO 2965:2009 is at least 1.5 times the air permeability of the second sorption element. More preferably, the air permeability of the first sorption element as measured in accordance with ISO 2965:2009 is at least 2 times the air permeability of the second sorption element.

In certain embodiments, the air permeability of the first sorption element as measured in accordance with ISO 2965:2009 may be between about 1.5 times and about 10 times the air permeability of the second sorption element, preferably between about 1.5 times and about 5 times the air permeability of the second sorption element. In other embodiments, the air permeability of the first sorption element as measured in accordance with ISO 2965:2009 may be between about 2 times and about 10 times the air permeability of the second sorption element, preferably between about 2 times and about 5 times the air permeability of the second sorption element.

In certain preferred embodiments the first sorption element may have an air permeability of between about 250 Coresta units and about 300 Coresta units as measured in accordance with ISO 2965:2009 and the second sorption element may have an air permeability of between about 100 Coresta units and about 150 Coresta units as measured in accordance with ISO 2965:2009.

The air permeability in Coresta units is the amount of air in cubic centimetres that passes through one square centimetre of the sorption element in one minute at a constant pressure difference of one kilopascal (that is, 1 Coresta unit corresponds to an air permeability of $1 \text{ cm}^3/\text{min} \cdot \text{cm}^2$ at a pressure differential of 1 kPa).

Alternatively or in addition, the porosity of the first sorption element may be greater than the porosity of the second sorption element. In such embodiments the increased porosity of the first sorption element relative to the second sorption element may increase the rate of release of

the delivery enhancing compound from the first sorption element relative to the rate of release of the delivery enhancing compound from the second sorption element.

Preferably, the porosity of the first sorption element as measured by mercury porosimetry in accordance with ISO 15901-1:2005 is at least 1.5 times the porosity of the second sorption element. More preferably, the porosity of the first sorption element as measured by mercury porosimetry is at least two times the porosity of the second sorption element.

In certain preferred embodiments the first sorption element may have a porosity of between about 20% and about 50% as measured by mercury porosimetry in accordance with ISO 15901-1:2005 and the second sorption element may have a porosity of between about 5% and about 35% as measured by mercury porosimetry in accordance with ISO 15901-1:2005.

In certain embodiments, the porosity of the first sorption element as measured by mercury porosimetry in accordance with ISO 15901-1:2005 may be between about 1.5 times and about 10 times the porosity of the second sorption element, preferably between about 1.5 times and about 5 times the porosity of the second sorption element. In other embodiments, the porosity of the first sorption element as measured by mercury porosimetry in accordance with ISO 15901-1:2005 may be between about 2 times and about 10 times the porosity of the second sorption element, preferably between about 2 times and about 5 times the porosity of the second sorption element.

Alternatively or in addition, the polarity of the second sorption element may be greater than the polarity of the first sorption element. This is particularly preferred where the volatile delivery enhancing compound is a polar compound. In such embodiments the increased polarity of the second sorption element relative to the first sorption element may decrease the rate of release of the delivery enhancing compound from the second sorption element relative to the rate of release of the delivery enhancing compound from the first sorption element.

The second sorption element may be immediately downstream of and in contact with the first sorption element.

Alternatively, the second sorption element may be spaced apart from the first sorption element.

Preferably, the volatile delivery enhancing compound has a vapour pressure of at least about 50 Pa, more preferably at least about 75 Pa, most preferably at least 100 Pa at 25°C.

Preferably, the volatile delivery enhancing compound has a vapour pressure of less than or equal to about 400 Pa, more preferably less than or equal to about 300 Pa, even more preferably less than or equal to about 275 Pa, most preferably less than or equal to about 250 Pa at 25°C.

In certain embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 20 Pa and about 400 Pa, more preferably between about 20 Pa and

about 300 Pa, even more preferably between about 20 Pa and about 275 Pa, most preferably between about 20 Pa and about 250 Pa at 25°C.

In other embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 50 Pa and about 400 Pa, more preferably between about 50 Pa and about 300 Pa, even more preferably between about 50 Pa and about 275 Pa, most preferably between about 50 Pa and about 250 Pa at 25°C.

In further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 75 Pa and about 400 Pa, more preferably between about 75 Pa and about 300 Pa, even more preferably between about 75 Pa and about 275 Pa, most preferably between about 75 Pa and about 250 Pa at 25°C.

In yet further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 100 Pa and about 400 Pa, more preferably between about 100 Pa and about 300 Pa, even more preferably between about 100 Pa and about 275 Pa, most preferably between about 100 Pa and about 250 Pa at 25°C.

The volatile delivery enhancing compound may comprise a single compound. Alternatively, the volatile delivery enhancing compound may comprise two or more different compounds.

Where the volatile delivery enhancing compound comprises two or more different compounds, the two or more different compounds in combination have a vapour pressure of at least about 20 Pa at 25°C.

Preferably, the volatile delivery enhancing compound is a volatile liquid.

The volatile delivery enhancing compound may comprise a mixture of two or more different liquid compounds.

The volatile delivery enhancing compound may comprise an aqueous solution of one or more compounds. Alternatively the volatile delivery enhancing compound may comprise a non-aqueous solution of one or more compounds.

The volatile delivery enhancing compound may comprise two or more different volatile compounds. For example, the volatile delivery enhancing compound may comprise a mixture of two or more different volatile liquid compounds.

Alternatively, the volatile delivery enhancing compound may comprise one or more non-volatile compounds and one or more volatile compounds. For example, the volatile delivery enhancing compound may comprise a solution of one or more non-volatile compounds in a volatile solvent or a mixture of one or more non-volatile liquid compounds and one or more volatile liquid compounds.

In one embodiment, the volatile delivery enhancing compound comprises an acid. The volatile delivery enhancing compound may comprise an organic acid or an inorganic acid.

Preferably, the volatile delivery enhancing compound comprises an organic acid, more preferably a carboxylic acid, most preferably an alpha-keto or 2-oxo acid.

In a preferred embodiment, the volatile delivery enhancing compound comprises an acid selected from the group consisting of 3-methyl-2-oxopentanoic acid, pyruvic acid, 2-oxopentanoic acid, 4-methyl-2-oxopentanoic acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof. In a particularly preferred embodiment, the volatile delivery enhancing compound comprises pyruvic acid.

Preferably, the delivery enhancing compound is adsorbed on the first sorption element and the second sorption element.

The first sorption element and the second sorption element act as reservoirs for the volatile delivery enhancing compound.

The first sorption element and the second sorption element may be formed from the same or different materials.

The first sorption element and the second sorption element may be formed from any suitable material or combination of materials. For example, the first sorption element and the second sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and BAREX®.

In a preferred embodiment, at least one of the first sorption element and the second sorption element is a porous sorption element.

For example, at least one of the first sorption element and the second sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

In a particularly preferred embodiment, both the first sorption element and the second sorption element are porous sorption elements.

The first sorption element and the second sorption element are preferably chemically inert with respect to the volatile delivery enhancing compound.

The first sorption element and the second sorption element may have any suitable shape and dimensions.

The first sorption element and the second sorption element may have the same or different shape and dimensions. Preferably, the first sorption element and the second sorption element are of the substantially the shape and dimensions.

In one embodiment, at least one of the first sorption element and the second sorption element is a cylindrical plug. In one preferred embodiment, at least one of the first sorption element and the second sorption element is a porous substantially cylindrical plug. In one

particularly preferred embodiment, both the first sorption element and the second sorption element are porous substantially cylindrical plugs.

In another embodiment, at least one of the first sorption element and the second sorption element is a substantially cylindrical hollow tube. In another preferred embodiment, at least one of the first sorption element and the second sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the first sorption element and the second sorption element may be chosen to allow a desired amount of the volatile delivery enhancing compound to be sorbed on the first sorption element and the second sorption element.

Preferably, the volatile delivery enhancing compound source comprises a total of between about 200 μ l and about 600 μ l, more preferably between about 250 μ l and about 550 μ l, most preferably between about 300 μ l and about 500 μ l of the volatile delivery enhancing compound.

The first sorption element and the second sorption element act as reservoirs for the volatile delivery enhancing compound.

Preferably, the amount of the volatile delivery enhancing compound adsorbed on the first sorption element is greater than the amount of the volatile delivery enhancing compound adsorbed on the second sorption element. In such embodiments the first sorption element advantageously acts as a main reservoir of the volatile delivery enhancing compound and the second sorption element acts as a minor reservoir of the volatile delivery enhancing compound.

Preferably, at least about 150 μ l, more preferably at least about 200 μ l, most preferably at least about 250 μ l of the volatile delivery enhancing compound is sorbed on the first sorption element.

For example, between about 150 μ l and about 450 μ l, more preferably between about 200 μ l and about 400 μ l, most preferably between about 225 μ l and about 375 μ l of the volatile delivery enhancing compound may be sorbed on the first sorption element.

Preferably, at least about 20 μ l, more preferably at least about 50 μ l, most preferably at least about 75 μ l of the volatile delivery enhancing compound is sorbed on the second sorption element.

For example, between about 20 μ l and about 200 μ l, more preferably between about 50 μ l and about 150 μ l, most preferably between about 75 μ l and about 125 μ l of the volatile delivery enhancing compound may be sorbed on the second sorption element.

The medicament source preferably comprises a medicament having a melting point below about 150 degrees Celsius. Alternatively or in addition, preferably the medicament has a boiling point below about 300 degrees Celsius.

In certain preferred embodiments, the medicament comprises one or more aliphatic or aromatic, saturated or unsaturated nitrogenous bases (nitrogen containing alkaline compounds) in which a nitrogen atom is present in a heterocyclic ring or in an acyclic chain (substitution).

The medicament may comprise one or more compounds selected from the group consisting of: nicotine; 7-Hydroxymitragynine; Arecoline; Atropine; Bupropion; Cathine (D-norpseudoephedrine); Chlorpheniramine; Dibucaine; Dimemorphan, Dimethyltryptamine, Diphenhydramine, Ephedrine, Hordenine, Hyoscyamine, Isoarecoline, Levorphanol, Lobeline, Mesembrine, Mitragynine, Muscatine, Procaine, Pseudo ephedrine, Pylamine, Raclopride, Ritodrine, Scopolamine, Sparteine (Lupinidine) and Ticlopidine; tobacco smoke constituents, such as 1,2,3,4 Tetrahydroisoquinolines, Anabasine, Anatabine, Cotinine, Myosmine, Nicotrine, Norcotinine, and Nornicotine; anti-asthmatic drugs, such as Orciprenaline, Propranolol and Terbutaline; anti-angina drugs, such as Nicorandil, Oxprenolol and Verapamil; antiarrhythmic drugs, such as Lidocaine; nicotinic agonists, such as Epibatidine, 5-(2R)-azetidylmethoxy)-2-chloropyridine (ABT-594), (S)-3-methyl-5-(1-methyl-2-pyrrolidinyl)isoxazole (ABT 418) and ($\pm$)-2-(3-Pyridinyl)-1-azabicyclo[2.2.2]octane (RJR-2429); nicotinic antagonists, such as Methyllycacinine and Mecamylamine; acetyl cholinesterase inhibitors, such as Galantamine, Pyridostigmine, Physostigmine and Tacrine; and MAO-inhibitors, such as Methoxy-N,N-dimethyltryptamine, 5-methoxy- α -methyltryptamine, Alpha-methyltryptamine, Iproclozide, Iproniazide, Isocarboxazide, Linezolid, Meclobemide, N,N- Dimethyltryptamine, Phenelzine, Phenyl ethylamine, Toloxatone, Tranylcypromine and Tryptamine.

In preferred embodiments, the medicament source is a nicotine source.

The nicotine source may comprise one or more of nicotine, nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate, or a nicotine derivative.

The nicotine source may comprise natural nicotine or synthetic nicotine.

The nicotine source may comprise pure nicotine, a solution of nicotine in an aqueous or non-aqueous solvent or a liquid tobacco extract.

The nicotine source may further comprise an electrolyte forming compound. The electrolyte forming compound may be selected from the group consisting of alkali metal hydroxides, alkali metal oxides, alkali metal salts, alkaline earth metal oxides, alkaline earth metal hydroxides and combinations thereof.

For example, the nicotine source may comprise an electrolyte forming compound selected from the group consisting of potassium hydroxide, sodium hydroxide, lithium oxide, barium oxide, potassium chloride, sodium chloride, sodium carbonate, sodium citrate, ammonium sulfate and combinations thereof

In certain embodiments, the nicotine source may comprise an aqueous solution of nicotine, nicotine base, a nicotine salt or a nicotine derivative and an electrolyte forming compound.

Alternatively or in addition, the nicotine source may further comprise other components including, but not limited to, natural flavours, artificial flavours and antioxidants.

The medicament source may comprise a third sorption element and a medicament sorbed on the third sorption element. In preferred embodiments where the medicament source is a nicotine source, the nicotine source may comprise a third sorption element and nicotine sorbed on the third sorption element.

The third sorption element acts as a reservoir for the nicotine or other medicament.

The third sorption element may be formed from the same or different materials to the first sorption element and the second sorption element.

The third sorption element may be formed from any suitable material or combination of materials. For example, the third sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and BAREX®.

In a preferred embodiment, the third sorption element is a porous sorption element.

For example, the third sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

The third sorption element is preferably chemically inert with respect to the nicotine or other medicament.

The third sorption element may have any suitable shape and dimensions.

The third sorption element may have the same or different shape and dimensions to the first sorption element and the second sorption element.

In one embodiment, the third sorption element is a cylindrical plug. In one preferred embodiment, the third sorption element is a porous substantially cylindrical plug.

In another embodiment, the third sorption element is a substantially cylindrical hollow tube. In another preferred embodiment, the third sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the third sorption element may be chosen to allow a desired amount of the nicotine or other medicament to be sorbed on the third sorption element.

Preferably, the medicament source comprises between about 10 µl and about 300 µl, more preferably between about 20 µl and about 200 µl, most preferably between about 50 µl and about 250 µl of the nicotine or other medicament.

In a preferred embodiment the aerosol-generating system comprises: an aerosol-generating article comprising the medicament source and the volatile delivery enhancing compound source.

Preferably, the aerosol-generating article comprises: a first compartment comprising a first one of the medicament source and the volatile delivery enhancing compound source; and a second compartment comprising a second one of the medicament source and the volatile delivery enhancing compound source.

5 Preferably, the first compartment comprises the volatile delivery enhancing compound source and the second compartment comprises the medicament source. However, it will be appreciated that the first compartment may alternatively comprise the medicament source and the second compartment may alternatively comprise the volatile delivery enhancing compound source.

10 The first compartment and the second compartment of the aerosol-generating article may abut one another. Alternatively, the first compartment and the second compartment of the aerosol-generating article may be spaced apart from one another.

 The first compartment of the aerosol-generating article may be sealed by one or more frangible barriers. In a preferred embodiment, the first compartment is sealed by a pair of
15 opposed transverse frangible barriers.

 Alternatively or in addition, the second compartment of the aerosol-generating article may be sealed by one or more frangible barriers. In a preferred embodiment, the second compartment is sealed by a pair of opposed transverse frangible barriers.

 The one or more frangible barriers may be formed from any suitable material. For
20 example, the one or more frangible barriers may be formed from a metal foil or film.

 The volume of the first compartment and the second compartment may be the same or different. In a preferred embodiment, the volume of the second compartment is greater than the volume of the first compartment.

 As described further below, the first compartment and the second compartment may be
25 arranged in series or parallel within the aerosol-generating article.

 As used herein, by "series" it is meant that the first compartment and the second compartment are arranged within the aerosol-generating article so that in use an air stream drawn through the aerosol-generating article passes through one of the first compartment and the second compartment and then passes through the other of the first compartment and the
30 second compartment.

 In embodiments in which the first compartment comprises the volatile delivery enhancing compound source and the second compartment comprises the medicament source, volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the first compartment into the air stream drawn through the aerosol-
35 generating article and medicament vapour is released from the medicament source in the second compartment into the air stream drawn through the aerosol-generating article. The

volatile delivery enhancing compound vapour reacts with the medicament vapour in the gas phase to form an aerosol, which is delivered to a user.

In embodiments in which the first compartment comprises the medicament source and the second compartment comprises the volatile delivery enhancing compound source, medicament vapour is released from the medicament source in the first compartment into the air stream drawn through the aerosol-generating article and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment into the air stream drawn through the aerosol-generating article. The medicament vapour reacts with the volatile delivery enhancing compound vapour in the gas phase to form an aerosol, which is delivered to a user.

Where the first compartment and the second compartment are arranged in series within the aerosol-generating article, the second compartment is preferably downstream of the first compartment so that in use an air stream drawn through the aerosol-generating article passes through the first compartment and then passes through the second compartment. However, it will be appreciated that the second compartment may alternatively be upstream of the first compartment so that in use an air stream drawn through the aerosol-generating article passes through the second compartment and then passes through the first compartment.

In embodiments where the second compartment is downstream of the first compartment, the volatile delivery enhancing compound vapour may react with the medicament vapour in the second compartment. In such embodiments the aerosol-generating article may further comprise a third compartment downstream of the second compartment and the volatile delivery enhancing compound vapour may alternatively or in addition react with the medicament vapour in the third compartment to form an aerosol.

In embodiments where the second compartment is upstream of the first compartment, the volatile delivery enhancing compound vapour may react with the medicament vapour in the first compartment. In such embodiments the aerosol-generating article may further comprise a third compartment downstream of the first compartment and the volatile delivery enhancing compound vapour may alternatively or in addition react with the medicament vapour in the third compartment to form an aerosol.

As used herein, by "parallel" it is meant that the first compartment and the second compartment are arranged within the aerosol-generating article so that in use a first air stream drawn through the aerosol-generating article passes through the first compartment and a second air stream drawn through the aerosol-generating article passes through the second compartment.

In embodiments in which the first compartment comprises the volatile delivery enhancing compound source and the second compartment comprises the medicament source, volatile delivery enhancing compound vapour is released from the volatile delivery enhancing

compound source in the first compartment into the first air stream drawn through the aerosol-generating article and medicament vapour is released from the medicament source in the second compartment into the second air stream drawn through the aerosol-generating article. The volatile delivery enhancing compound vapour in the first air stream reacts with the medicament vapour in the second air stream in the gas phase to form an aerosol, which is delivered to a user.

In such embodiments the aerosol-generating article may further comprise a third compartment downstream of the first compartment and the second compartment and the volatile delivery enhancing compound vapour in the first air stream may mix and react with the medicament vapour in the second air stream in the third compartment to form an aerosol.

In embodiments in which the first compartment comprises the medicament source and the second compartment comprises the volatile delivery enhancing compound source, medicament vapour is released from the medicament source in the first compartment into the first air stream drawn through the aerosol-generating article and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment into the second air stream drawn through the aerosol-generating article. The medicament vapour in the first air stream reacts with the volatile delivery enhancing compound vapour in the second air stream in the gas phase to form an aerosol, which is delivered to a user.

In such embodiments the aerosol-generating article may further comprise a third compartment downstream of the first compartment and the second compartment and the medicament vapour in the first air stream may mix and react with the volatile delivery enhancing compound vapour in the second air stream in the third compartment to form an aerosol.

In particularly preferred embodiments, the aerosol-generating article comprises: a housing comprising: an air inlet; a first compartment in communication with the air inlet, the first compartment comprising a first one of the medicament source and the volatile delivery enhancing compound source; a second compartment in communication with the first compartment, the second compartment comprising a second one of the medicament source and the volatile delivery enhancing compound source; and an air outlet, wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

As used herein, the term "air inlet" is used to describe one or more apertures through which air may be drawn into the aerosol-generating article.

As used herein, the term "air outlet" is used to describe one or more apertures through which air may be drawn out of the aerosol-generating article.

In such embodiments, the first compartment and the second compartment are arranged in series from air inlet to air outlet within the housing. That is, the first compartment is

downstream of the air inlet, the second compartment is downstream of the first compartment and the air outlet is downstream of the second compartment. In use, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment and the second compartment and out of the housing through the air outlet.

5 The aerosol-generating article may further comprise a third compartment in communication with: the second compartment; and the air outlet. In use in such embodiments, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment, the second compartment and the third compartment and out of the housing through the air outlet.

10 The aerosol-generating article may further comprise a mouthpiece in communication with: the second compartment or the third compartment, where present; and the air outlet. In use in such embodiments, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment, the second compartment, the third compartment, where present, and the mouthpiece and out of the housing through the air outlet.

15 In other preferred embodiments, the aerosol-generating article comprises: a housing comprising: an air inlet; a first compartment in communication with the air inlet, the first compartment comprising a first one of the medicament source and the volatile delivery enhancing compound source; a second compartment in communication with the air inlet, the second compartment comprising a second one of the medicament source and the volatile
20 delivery enhancing compound source; and an air outlet, wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

In such embodiments, the first compartment and the second compartment are arranged in parallel from air inlet to air outlet within the housing. The first compartment and the second
25 compartment are both downstream of the air inlet and upstream of the air outlet. In use, a stream of air is drawn into the housing through the air inlet, a first portion of the stream of air is drawn downstream through the first compartment and a second portion of the stream of air is drawn downstream through the second compartment.

The aerosol-generating article may further comprise a third compartment in
30 communication with: one or both of the first compartment and the second compartment; and the air outlet.

The aerosol-generating article may further comprise a mouthpiece in communication with: the first compartment and the second compartment, or the third compartment, where present; and the air outlet.

35 In further preferred embodiments, the aerosol-generating article comprises: a housing comprising: a first air inlet; a second air inlet; a first compartment in communication with the first air inlet, the first compartment comprising a first one of the medicament source and the volatile

delivery enhancing compound source; a second compartment in communication with the second air inlet, the second compartment comprising a second one of the medicament source and the volatile delivery enhancing compound source; and an air outlet, wherein the first air inlet, the second air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the first air inlet, through the housing and out of the housing through the air outlet and air may pass into the housing through the second air inlet, through the housing and out of the housing through the air outlet.

In such embodiments, the first compartment and the second compartment are arranged in parallel within the housing. The first compartment is downstream of the first air inlet and upstream of the air outlet and the second compartment is downstream of the second air inlet and upstream of the air outlet. In use, a first stream of air is drawn into the housing through the first air inlet and downstream through the first compartment and a second stream of air is drawn into the housing through the second air inlet and downstream through the second compartment.

The aerosol-generating article may further comprise a third compartment in communication with: one or both of the first compartment and the second compartment; and the air outlet.

The aerosol-generating article may further comprise a mouthpiece in communication with: the first compartment and the second compartment, or the third compartment, where present; and the air outlet.

The housing of the aerosol-generating article may simulate the shape and dimensions of a tobacco smoking article, such as a cigarette, a cigar, a cigarillo or a pipe, or a cigarette pack. In a preferred embodiment, the housing simulates the shape and dimensions of a cigarette.

Where present, the third compartment may comprise one or more aerosol-modifying agents. For example, the third compartment may comprise an adsorbent, such as activated carbon, a flavourant, such as menthol, or a combination thereof.

Where present, the mouthpiece may comprise a filter. The filter may have a low particulate filtration efficiency or very low particulate filtration efficiency. Alternatively, the mouthpiece may comprise a hollow tube.

In a preferred embodiment the aerosol-generating system comprises: an aerosol-generating article comprising the medicament source and the volatile delivery enhancing compound source; and an aerosol-generating device in cooperation with the aerosol-generating article, the aerosol generating device comprising heating means for heating one or both of the medicament source and the volatile delivery enhancing compound source of the aerosol-generating article.

The aerosol-generating device preferably comprises a cavity configured to receive at least a portion of the aerosol-generating article.

In embodiments where the aerosol-generating article comprises: a first compartment comprising a first one of the medicament source and the volatile delivery enhancing compound source; and a second compartment comprising a second one of the medicament source and the volatile delivery enhancing compound source, the aerosol-generating device preferably comprises a cavity configured to receive the first compartment and the second compartment of the aerosol-generating article.

Preferably, the cavity of the aerosol-generating device is substantially cylindrical.

The cavity of the aerosol-generating device may have a transverse cross-section of any suitable shape. For example, the cavity may be of substantially circular, elliptical, triangular, square, rhomboidal, trapezoidal, pentagonal, hexagonal or octagonal transverse cross-section.

As used herein, the term "transverse cross-section" is used to describe the cross-section of the cavity perpendicular to the major axis of the cavity.

Preferably, the cavity of the aerosol-generating device has a transverse cross-section of substantially the same shape as the transverse cross-section of the aerosol-generating article.

In certain embodiments, the cavity of the aerosol-generating device may have a transverse cross-section of substantially the same shape and dimensions as the transverse cross-section of the aerosol-generating article to be received in the cavity in order to maximize conductive thermal transfer from the aerosol-generating device to the aerosol-generating article.

Preferably, the cavity of the aerosol-generating device is of substantially circular transverse cross-section or of substantially elliptical transverse cross-section. Most preferably, the cavity of the aerosol-generating device is of substantially circular transverse cross-section.

Preferably, the length of the cavity of the aerosol-generating device is less than the length of the aerosol-generating article so that when the aerosol-generating article is received in the cavity of the aerosol-generating device the proximal or downstream end of the aerosol-generating article projects from the cavity of the aerosol-generating device.

As used herein, by "length" is meant the maximum longitudinal dimension between the distal or upstream end and the proximal or downstream end of the cavity and aerosol-generating article.

Preferably, the cavity of the aerosol-generating device has a diameter substantially equal to or slightly greater than the diameter of the aerosol-generating article.

As used herein, by "diameter" is meant the maximum transverse dimension of the cavity and aerosol-generating article.

In embodiments where one or both of the first compartment and the second compartment of the aerosol-generating article is sealed by one or more frangible seals, the aerosol-generating device may further comprise a piercing member positioned within the cavity for piercing the first and second compartments of the aerosol-generating article. The piercing member may be formed from any suitable material.

Where the first compartment and the second compartment of the aerosol-generating article are arranged in series within the aerosol-generating article, the piercing member is preferably positioned centrally within the cavity of the aerosol-generating device, along the major axis of the cavity.

5 Where the first compartment and the second compartment of the aerosol-generating article are arranged in parallel within the aerosol-generating article, the piercing member may comprise a first piercing element positioned within the cavity of the aerosol-generating device for piercing the first compartment of the aerosol-generating article and a second piercing
10 element positioned within the cavity of the aerosol-generating device for piercing the second compartment of the aerosol-generating article.

The aerosol generating device comprises heating means for heating one or both of the medicament source and the volatile delivery enhancing compound source of the aerosol-generating article.

The heating means may be a non-electrical heating means.

15 In certain embodiments the heating means may comprise a heat sink or heat exchanger configured to transfer thermal energy from an external heat source to one or both of the medicament source and the volatile delivery enhancing compound source of the aerosol-generating article. The heat sink or heat exchanger may be formed of any suitable thermally conductive material. Suitable materials include, but are not limited to, metals, such as
20 aluminium and copper.

In certain embodiments, the heating means may comprise a heat sink or heat exchanger configured to transfer thermal energy from a blue flame or torch lighter or other lighter to one or both of the medicament source and the volatile delivery enhancing compound source of the aerosol-generating article. In such embodiments, a user may advantageously use a lighter to
25 activate the aerosol-generating system in a manner similar to lighting a cigarette or other conventional smoking article.

The heat sink or heat exchanger may extend fully or partially along the length of the cavity of the aerosol-generating device.

Alternatively, the heating means may be an electrical heating means powered by an
30 electric power supply.

Where the heating means is an electric heating means, the aerosol-generating device may further comprise an electric power supply and a controller comprising electronic circuitry configured to control the supply of electric power from the electric power supply to the electric heating means. Any suitable electronic circuitry may be used in order to control the supply of
35 power to the electric heating means. The electronic circuitry may be programmable.

Alternatively, the electrical heating means may be powered by an external electric power supply.

The electric power supply may be a DC voltage source. In preferred embodiments, the electric power supply is a battery. For example, the electric power supply may be a Nickel-metal hydride battery, a Nickel cadmium battery, or a Lithium based battery, for example a Lithium-Cobalt, a Lithium-Iron-Phosphate or a Lithium-Polymer battery. The electric power supply may alternatively be another form of electric charge storage device such as a capacitor. The electric power supply may require recharging and may have a capacity that allows for the storage of enough electrical energy for use of the aerosol-generating device with one or more aerosol-generating articles.

The aerosol-generating device may comprise a heating means comprising one or more heating elements. The one or more heating elements may extend fully or partially along the length of the cavity of the aerosol-generating device. The one or more heating elements may extend fully or partially around the circumference of the cavity of the aerosol-generating device.

The aerosol-generating device may further comprise a controller configured to independently control a supply of power to the one or more heating elements.

In one preferred embodiment the heating means comprises one or more heating elements that are heated electrically. However, other heating schemes may be used to heat the one or more heating elements. For example, the one or more heating elements may be heated by conduction from another heat source. Alternatively, the one or more heating elements may be infra-red heating elements or inductive heating elements.

In a particularly preferred embodiment, the heating means comprises one or more heating elements comprising an electrically resistive material. Each heating element may comprise a non-elastic material, for example a ceramic sintered material, such as alumina (Al_2O_3) and silicon nitride (Si_3N_4), or printed circuit board or silicon rubber. Alternatively, each heating element may comprise an elastic, metallic material, for example an iron alloy or a nickel-chromium alloy. The one or more heating elements may be flexible heating foils on a dielectric substrate, such as polyimide. Alternatively, the one or more heating elements may be metallic grid or grids, flexible printed circuit boards, or flexible carbon fibre heaters.

Other suitable electrically resistive materials include but are not limited to: semiconductors such as doped ceramics, electrically "conductive" ceramics (such as, for example, molybdenum disilicide), carbon, graphite, metals, metal alloys and composite materials made of a ceramic material and a metallic material. Such composite materials may comprise doped or undoped ceramics. Examples of suitable doped ceramics include doped silicon carbides. Examples of suitable metals include titanium, zirconium, tantalum and metals from the platinum group. Examples of suitable metal alloys include stainless steel, nickel-, cobalt-, chromium-, aluminium- titanium- zirconium-, hafnium-, niobium-, molybdenum-, tantalum-, tungsten-, tin-, gallium- and manganese- alloys, and super-alloys based on nickel, iron, cobalt, stainless steel, Timetal® and iron-manganese-aluminium based alloys. Timetal® is

a registered trade mark of Titanium Metals Corporation, 1999 Broadway Suite 4300, Denver, Colorado. In composite materials, the electrically resistive material may optionally be embedded in, encapsulated or coated with an insulating material or vice-versa, depending on the kinetics of energy transfer and the external physicochemical properties required.

5 The aerosol-generating device may further comprise a temperature sensor configured to sense the temperature of the aerosol-generating device.

In such embodiments, the aerosol-generating device may comprise a controller configured to control a supply of power to the one or more heating elements based on the temperature of the aerosol-generating article sensed by the temperature sensor.

10 The heating means may comprise one or more heating elements formed using a metal having a defined relationship between temperature and resistivity. In such embodiments, the metal may be formed as a track between two layers of suitable insulating materials. Heating elements formed in this manner may be used to both heat and monitor the temperature of the aerosol-generating article.

15 The aerosol-generating device may further comprise a housing containing the cavity, heating means and, where present, controller, and power source.

Preferably, the housing of the aerosol-generating device is substantially cylindrical.

The housing of the aerosol-generating device may be designed to be grasped or held by a user.

20 In a preferred embodiment, the aerosol-generating device is a cylindrical heating sleeve.

For the avoidance of doubt, features described above in relation to one aspect of the invention may also be applicable to other aspects of the invention. In particular, features described above in relation to aerosol-generating systems according to the invention may also relate, where appropriate, to aerosol-generating articles according to the invention and vice versa.

25 The invention will now be further described with reference to the accompanying drawings in which:

Figure 1(a) shows a schematic longitudinal cross-section of an aerosol-generating article comprising a medicament source and a volatile delivery enhancing compound source of the type disclosed in WO 2008/121610 A1 and WO 2010/107613 A1.

Figure 1(b) shows a schematic longitudinal cross-section of an aerosol-generating article comprising a medicament source and a volatile delivery enhancing compound source according to a first embodiment of the invention;

Figure 1(c) shows a schematic longitudinal cross-section of an aerosol-generating article comprising a medicament source and a volatile delivery enhancing compound source according to a second embodiment of the invention;

Figure 2 shows the nicotine delivery per puff as a function of puff number for aerosol-generating articles according to: comparative example (a); example (b); and example (c) upon heating measured under a Health Canada smoking regime;

Figure 3 shows the nicotine delivery per puff as a function of puff number for aerosol-generating articles according to: example (b); example (d); and example (e) upon heating measured under a Health Canada smoking regime; and

Figure 4 shows the nicotine delivery per puff as a function of puff number for aerosol-generating articles according to: example (b); example (f); and example (g) upon heating measured under a Health Canada smoking regime.

The prior art aerosol-generating article shown in Figure 1(a) comprises a pyruvic acid source (10) and a nicotine source (20). As shown in Figure 1(a), the pyruvic acid source (10) and the nicotine source (20) are arranged in series with the nicotine source (20) downstream of and spaced apart from the pyruvic acid source (10). The pyruvic acid source (10) comprises a porous sorption element (30) with pyruvic acid sorbed thereon and the nicotine source (20) comprises a porous sorption element (50) with nicotine sorbed thereon.

The aerosol-generating article according to the first embodiment shown in Figure 1(b) also comprises a pyruvic acid source (10) and a nicotine source (20) arranged in series with the nicotine source (20) downstream of and spaced apart from the pyruvic acid source (10). However, the aerosol-generating article according to the first embodiment of the invention shown in Figure 1(b) differs from the prior art aerosol-generating article shown in Figure 1(a) in that the pyruvic acid source (10) comprises a first porous sorption element (30) with pyruvic acid sorbed thereon and a second porous sorption element (40) with pyruvic acid sorbed thereon. As shown in Figure 1(b), the first porous sorption element (30) and the second porous sorption element (40) are arranged in series with the second porous sorption element (40) immediately downstream of and abutting the first porous sorption element (30).

The aerosol-generating article according to the second embodiment of the invention shown in Figure 1(b) is of similar construction to the aerosol-generating article according to the first embodiment shown in Figure 1(b). However, in the aerosol-generating article according to the second embodiment shown in Figure 1(b) the second porous sorption element (40) of the pyruvic acid source (10) is downstream of and spaced apart from the first porous sorption element (30) of the pyruvic acid source (10).

Comparative example (a)

To form a pyruvic acid source 500 µl of pyruvic acid is sorbed by capillarity onto a sintered porous plastic plug with a length of 20 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

- 5 A prior art aerosol-generating article having the construction shown in Figure 1(a) is assembled comprising the pyruvic acid source and the nicotine source. The nicotine source is positioned 10 mm downstream of the pyruvic acid source.

Example (b)

- 10 To form a pyruvic acid source 250 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath and 100 µl of pyruvic acid is sorbed by capillarity onto a second sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene
15 terephthalate (PET) sheath and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany) and a suitable second porous plastic plug is Porex® XMF-0607 (available from Porex GmbH, Germany).

- 20 To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

- 25 An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned immediately downstream of and abutting the first sintered porous plastic plug of the pyruvic acid source and the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

Example (c)

- 30 To form a pyruvic acid source 250 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath and 100 µl of pyruvic acid is sorbed by capillarity onto a second sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene
35 terephthalate (PET) sheath and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-0507 (available from Porex GmbH,

Germany) and a suitable second porous plastic plug is Porex® XMF-0607 (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned 2 mm downstream of the first sintered porous plastic plug of the pyruvic acid source and the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

Example (d)

To form a pyruvic acid source 250 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath and 100 µl of pyruvic acid is sorbed by capillarity onto a second sintered porous plastic plug with a length of 10 mm and a density of 0.3g/cm³ having a polyethylene terephthalate (PET) core, a polyethylene (PE) sheath and a viscose B fibre filling and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany) and a suitable second sintered porous plastic plug is Porex® XMF-0130+B (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned immediately downstream of and abutting the first sintered porous plastic plug of the pyruvic acid source and the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

Example (e)

To form a pyruvic acid source 250 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a

polyethylene terephthalate (PET) core and a polyethylene (PE) sheath and 100 µl of pyruvic acid is sorbed by capillarity onto a second sintered porous plastic plug with a length of 10 mm and a density of 0.15g/cm³ having a polyethylene terephthalate (PET) core, a polyethylene (PE) sheath and a viscose B fibre filling and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany) and a suitable second sintered porous plastic plug is Porex® XMF-0130+B (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned immediately downstream of and abutting the first sintered porous plastic plug of the pyruvic acid source and the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

Example (f)

To form a pyruvic acid source 320 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.3g/cm³ having a polyethylene terephthalate (PET) core, a polyethylene (PE) sheath and a viscose B fibre filling sintered and 100 µl of pyruvic acid is sorbed by capillarity onto a second porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene terephthalate (PET) sheath and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-130+B (available from Porex GmbH, Germany) and a suitable second sintered porous plastic plug is Porex® XMF-607 (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned immediately downstream of and abutting the first sintered porous plastic plug of the pyruvic acid source and

the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

Example (g)

To form a pyruvic acid source 320 µl of pyruvic acid is sorbed by capillarity onto a first sintered porous plastic plug with a length of 10 mm and a density of 0.15g/cm³ having a polyethylene terephthalate (PET) core, a polyethylene (PE) sheath and a viscose B fibre filling sintered and 100 µl of pyruvic acid is sorbed by capillarity onto a second porous plastic plug with a length of 10 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene terephthalate (PET) sheath and a lower air permeability than the first sintered porous plastic plug. A suitable first porous plastic plug is Porex® XMF-130+B (available from Porex GmbH, Germany) and a suitable second sintered porous plastic plug is Porex® XMF-607 (available from Porex GmbH, Germany).

To form a nicotine source 10 µl of nicotine is sorbed by capillarity onto a sintered porous plastic plug with a length of 50 mm and a density of 0.33g/cm³ having a polyethylene terephthalate (PET) core and a polyethylene (PE) sheath. A suitable porous plastic plug is Porex® XMF-0507 (available from Porex GmbH, Germany).

An aerosol-generating article according to the invention having the construction shown in Figure 1(b) is assembled comprising the pyruvic acid source and the nicotine source. The second sintered porous plastic plug of the pyruvic acid source is positioned immediately downstream of and abutting the first sintered porous plastic plug of the pyruvic acid source and the nicotine source is positioned 10 mm downstream of the second sintered porous plastic plug of the pyruvic acid source.

The nicotine yield per group of five puffs of the aerosol-generating articles of comparative example (a) and examples (b) to (g) is measured under a Health Canada smoking regime over 30 puffs with a puff volume of 55 ml, puff duration of 2 seconds and a puff interval of 30 seconds. Each group of five puffs is collected on a Cambridge filter pad and then extracted with a liquid solvent. The resulting liquid is analysed by gas chromatography to determine the nicotine delivery. The results are shown in Figures 2, 3 and 4.

As shown in Figure 2, the nicotine delivery of puffs 6-10, 11-15, 16-20, 21-25 and 26-30 of the aerosol-generating articles according to the invention of examples (b) and (c) is greater than that of the corresponding puffs of the prior art aerosol-generating article of comparative example (a). As a result, the inclusion in the aerosol-generating articles according to the invention of examples (b) and (c) of a pyruvic acid source comprising a first porous sorption element and a second porous sorption element downstream of the first sorption element, wherein the rate of release of the pyruvic acid from the first sorption element is greater than the

rate of release of the pyruvic acid from the second sorption element, advantageously results in more consistent and sustained delivery of nicotine delivery compared to the prior art aerosol-generating article of comparative example (a).

5 As shown in Figures 3 and 4, altering the properties of the first sorption element and the second sorption element and hence the difference in the rate of release of the pyruvic acid from the first sorption element and the second sorption element advantageously allows the nicotine delivery of the aerosol-generating articles according to the invention in examples (b) to (g) to be controlled.

10 The invention has been exemplified above by reference to aerosol-generating articles comprising delivery enhancing compound sources comprising porous plastic plugs having pyruvic acid adsorbed thereon and medicament sources comprising porous plastic plugs having nicotine adsorbed thereon. However, it will be appreciated that aerosol-generating articles and aerosol-generating systems according to the invention may comprise other sorption elements, other delivery enhancing compounds and other medicaments.

15

CLAIMS:

1. An aerosol-generating system comprising:
a medicament source; and
5 a volatile delivery enhancing compound source, the volatile delivery enhancing compound source comprising:
a first sorption element;
a second sorption element downstream of the first sorption element; and
a volatile delivery enhancing compound sorbed on the first sorption element and
10 the second sorption element,
wherein the rate of release of the volatile delivery enhancing compound from the first sorption element is greater than the rate of release of the volatile delivery enhancing compound from the second sorption element.
- 15 2. An aerosol-generating system according to claim 1 wherein the air permeability of the first sorption element is greater than the air permeability of the second sorption element.
3. An aerosol-generating system according to claim 1 or 2 wherein the porosity of the first sorption element is greater than the porosity of the second sorption element.
20
4. An aerosol-generating system according to claim wherein the polarity of the second sorption element is greater than the polarity of the first sorption element.
5. An aerosol-generating system according to any one of claims 1 to 4 wherein the
25 medicament source comprises:
a third sorption element; and
a medicament sorbed on the first sorption element.
6. An aerosol-generating system according to claim 5 wherein the medicament comprises
30 nicotine.
7. An aerosol-generating system according to any one of claims 1 to 6 wherein the volatile delivery enhancing compound comprises an acid.
- 35 8. An aerosol-generating system according to claim 7 wherein the acid is selected from the group consisting of 3-methyl-2-oxovaleric acid, pyruvic acid, 2-oxovaleric acid, 4-methyl-2-oxovaleric acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof.

9. An aerosol-generating system according to claim 8 wherein the acid is pyruvic acid.
10. An aerosol-generating system according to any one of claims 1 to 9 wherein the amount of the volatile delivery enhancing compound sorbed on the first sorption element is greater than
5 the amount of the volatile delivery enhancing compound sorbed on the second sorption element.
11. An aerosol-generating system according to any one of claims 1 to 10 wherein the first sorption element is of substantially the same dimensions as the second sorption element.
10
12. An aerosol-generating system according to any one of claims 1 to 11 wherein the second sorption element is immediately downstream of and in contact with the first sorption element.
13. An aerosol-generating system according to any one of claims 1 to 12 wherein the
15 second sorption element spaced apart from the first sorption element.
14. An aerosol-generating system according to any one of claims 1 to 15 comprising:
an aerosol-generating article comprising the medicament source and the volatile delivery
20 enhancing compound source.
15. An aerosol-generating system according to claim 14 further comprising:
an aerosol-generating device in cooperation with the aerosol-generating article, the
aerosol generating device comprising heating means for heating one or both of the medicament
25 source and the volatile delivery enhancing compound source of the aerosol-generating article.
16. An aerosol-generating article for use in an aerosol-generating system according to claim 14 or 15.
17. An aerosol-generating article according to claim 16 comprising a housing comprising:
30 an air inlet;
a first compartment in communication with the air inlet, the first compartment comprising
a first one of the medicament source and the volatile delivery enhancing compound source;
a second compartment in communication with the first compartment, the second
35 compartment comprising a second one of the medicament source and the volatile delivery
enhancing compound source; and
an air outlet,

wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

- 5 18. An aerosol-generating article according to claim 16 comprising a housing comprising:
an air inlet;
a first compartment in communication with the air inlet, the first compartment comprising
a first one of the medicament source and the volatile delivery enhancing compound source;
a second compartment in communication with the air inlet, the second compartment
10 comprising a second one of the medicament source and the volatile delivery enhancing
compound source; and
an air outlet,

wherein the air inlet and the air outlet are in communication with each other and
configured so that air may pass into the housing through the air inlet, through the housing and
15 out of the housing through the air outlet.

19. An aerosol-generating article according to claim 16 comprising a housing comprising:
a first air inlet;
a second air inlet;
20 a first compartment in communication with the first air inlet, the first compartment
comprising a first one of the medicament source and the volatile delivery enhancing compound
source;
a second compartment in communication with the second air inlet, the second
compartment comprising a second one of the medicament source and the volatile delivery
25 enhancing compound source; and
an air outlet,

wherein the first air inlet, the second air inlet and the air outlet are in communication with
each other and configured so that air may pass into the housing through the first air inlet,
through the housing and out of the housing through the air outlet and air may pass into the
30 housing through the second air inlet, through the housing and out of the housing through the air
outlet.

20. An aerosol-generating article according to any one of claims 17 to 19 wherein one or
both of the first compartment and the second compartment of the aerosol-generating article is
35 sealed by one or more frangible seals.

21. An aerosol-generating article according to any one of claims 16 to 20 wherein the first compartment comprises the volatile delivery enhancing compound source and the second compartment comprises the nicotine source.

- 1/2 -

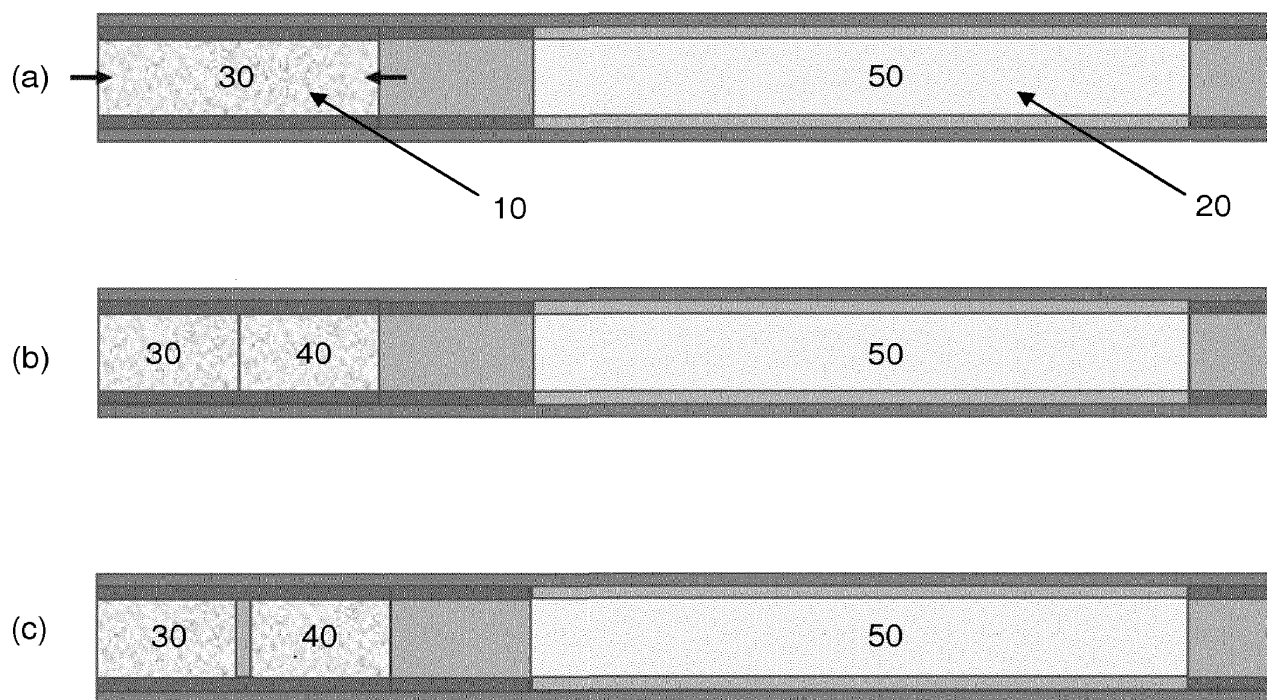


Figure 1

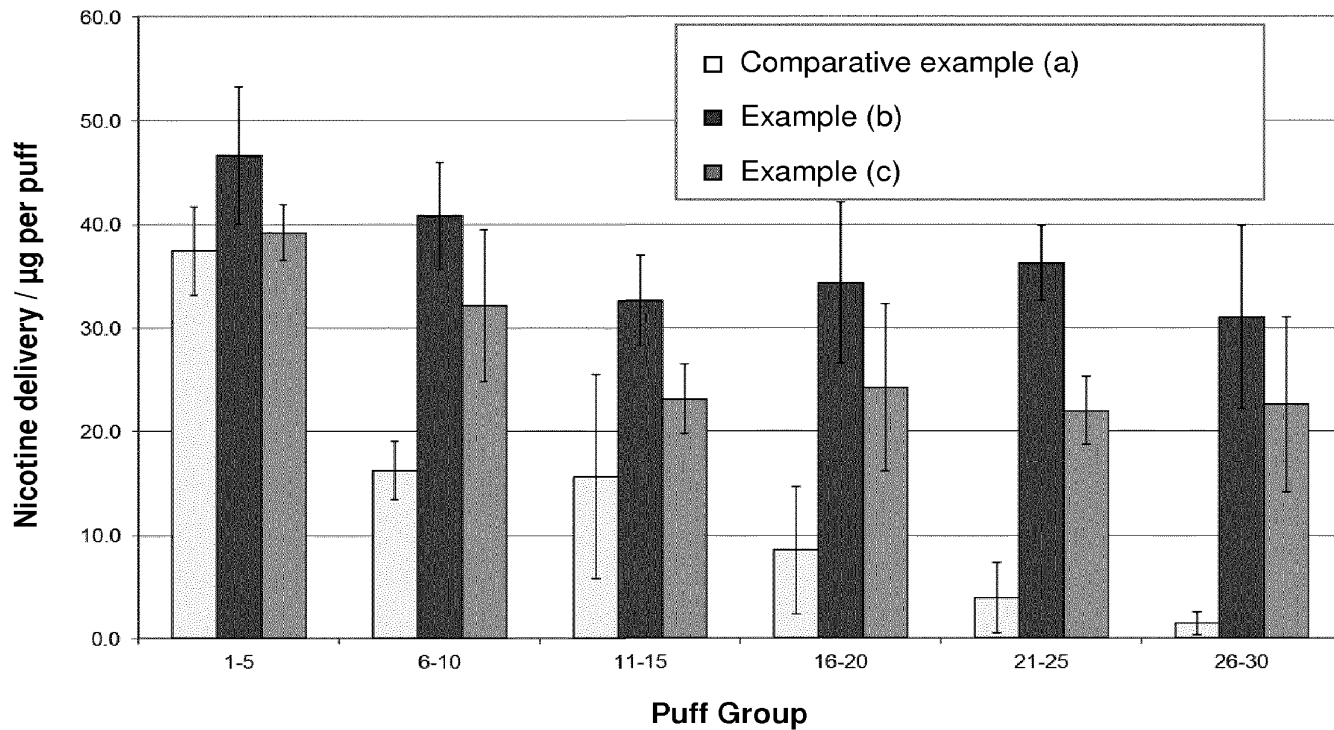


Figure 2

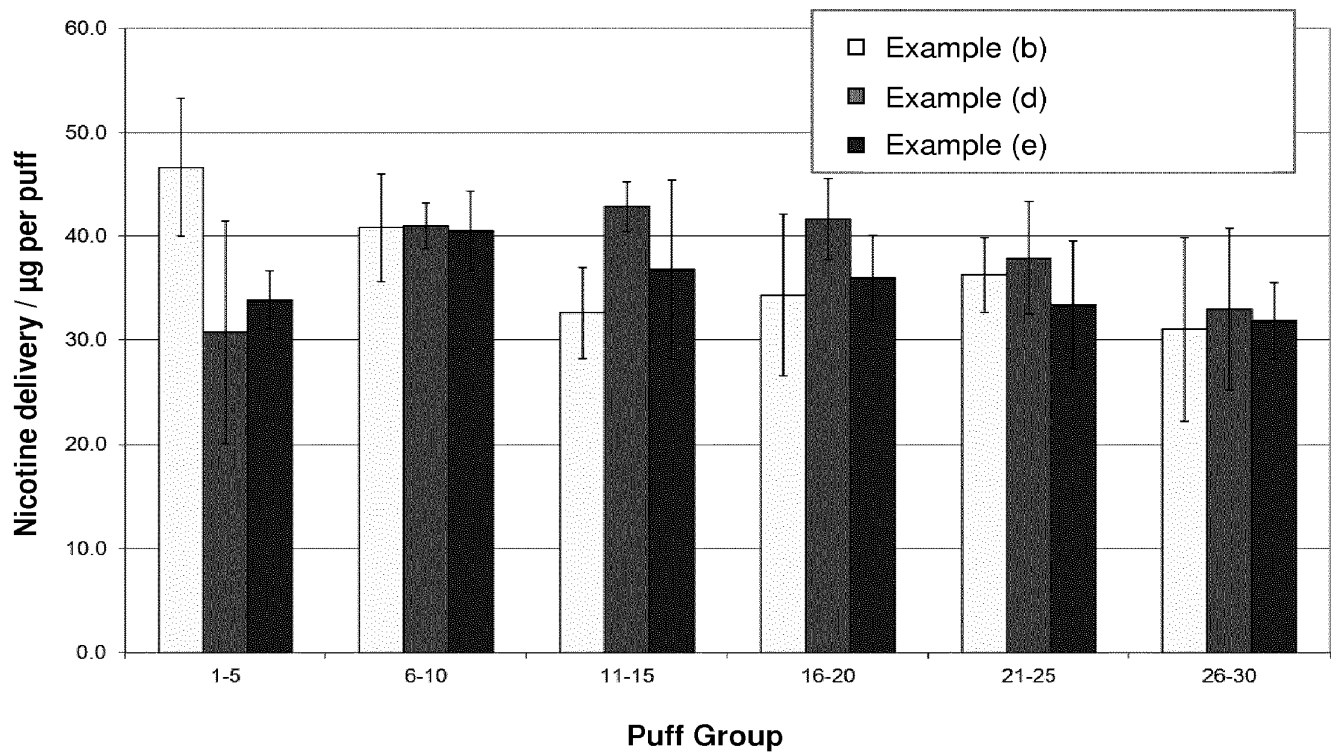


Figure 3

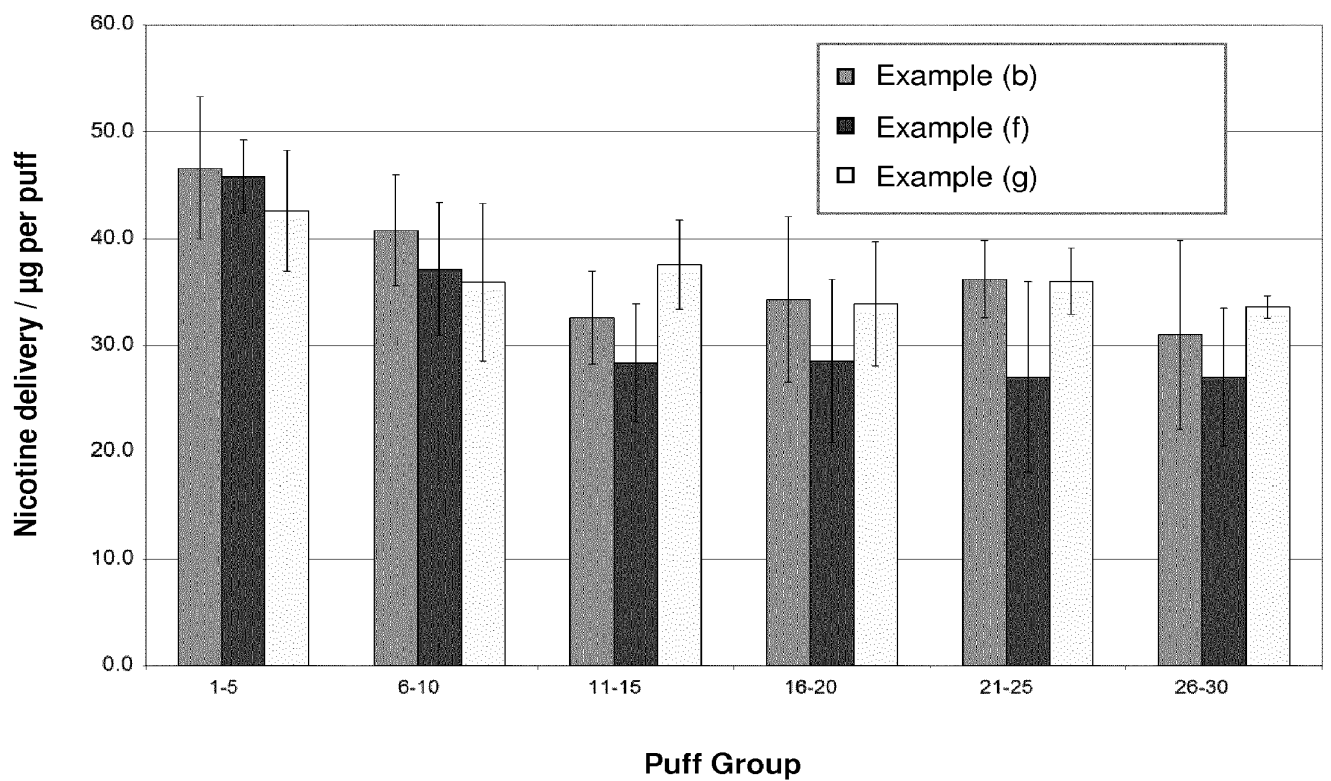


Figure 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/060204

A. CLASSIFICATION OF SUBJECT MATTER INV. A61M11/00 A61M15/00 A61M15/06 A24F47/00 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61M A24F		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/107613 A1 (UNIV DUKE [US]; ROSE SETH D [US]; TURNER JAMES EDWARD [US]; MURUGESAN) 23 September 2010 (2010-09-23) cited in the application	1-11,13,14,16-20
A	paragraph [0043] - paragraph [0082]; figures 2b,2c	12,21
A	----- US 5 546 965 A (WHITE JACKIE L [US]) 20 August 1996 (1996-08-20) figure 1	1-21
A	----- EP 0 354 661 A2 (BRITISH AMERICAN TOBACCO CO [GB]) 14 February 1990 (1990-02-14) paragraph [0027]; figure 1	1-21
A	----- US 4 830 028 A (LAWSON JERRY W [US] ET AL) 16 May 1989 (1989-05-16) column 3, line 29 - line 52; figure 1	1-21
<div style="display: flex; justify-content: space-between;"> ☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex. </div>		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents :</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search <div style="text-align: center; font-weight: bold;">3 June 2014</div>		Date of mailing of the international search report <div style="text-align: center; font-weight: bold;">12/06/2014</div>
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer <div style="text-align: center; font-weight: bold;">Louarn, Arzhur</div>

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/060204

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010107613	A1	23-09-2010	
		AU 2010226152 A1	06-10-2011
		CA 2755580 A1	23-09-2010
		CN 102355914 A	15-02-2012
		CO 6410316 A2	30-03-2012
		EP 2408494 A1	25-01-2012
		JP 2012520736 A	10-09-2012
		KR 20110139238 A	28-12-2011
		NZ 594585 A	31-01-2014
		RU 2011141824 A	27-04-2013
		SG 174867 A1	28-11-2011
		US 2012006342 A1	12-01-2012
		WO 2010107613 A1	23-09-2010

US 5546965	A	20-08-1996	NONE

EP 0354661	A2	14-02-1990	
		AT 151234 T	15-04-1997
		AU 633502 B2	04-02-1993
		AU 3894389 A	15-02-1990
		CA 1330922 C	26-07-1994
		DE 68927947 D1	15-05-1997
		DE 68927947 T2	28-08-1997
		EP 0354661 A2	14-02-1990
		EP 0712584 A2	22-05-1996
		ES 2100847 T3	01-07-1997
		GR 3023434 T3	29-08-1997
		US 5050621 A	24-09-1991

US 4830028	A	16-05-1989	
		JP H01104153 A	21-04-1989
		TR 23993 A	14-01-1991
		US 4830028 A	16-05-1989
		US 4836224 A	06-06-1989

Electronic Patent Application Fee Transmittal				
Application Number:		14925968		
Filing Date:		28-Oct-2015		
Title of Invention:		NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		
First Named Inventor/Applicant Name:		Adam BOWEN		
Filer:		Richard Douglas Shoop/Brian Flick		
Attorney Docket Number:		13211-713.303		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
Total in USD (\$)				180

Electronic Acknowledgement Receipt

EFS ID:	25212635
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	16-MAR-2016
Filing Date:	28-OCT-2015
Time Stamp:	14:03:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 180
RAM confirmation Number	309
Deposit Account	504050
Authorized User	SHOOP, RICHARD D

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_3-16-2016.pdf	2103622 896145fb4cf2d2d7f048b2e72da17f6bdc62267e	yes	23
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Transmittal Letter		1	3	
	Information Disclosure Statement (IDS) Form (SB08)		4	23	
Warnings:					
Information:					
2	Foreign Reference	CA2641869A1.pdf	1053466 2a674dfdee30ab3ce2e6399401620233b73514c7	no	28
Warnings:					
Information:					
3	Foreign Reference	CN101869356AwEngTrans.pdf	1713097 00f18d421b9b59b5c0737633cd930e2a2ffc5972	no	25
Warnings:					
Information:					
4	Foreign Reference	CN85106876AwCorresEng.pdf	7176242 93ff1ad4fd0c6c0981b0fde6171bb1e2ef5dc7a8	no	29
Warnings:					
Information:					
5	Foreign Reference	DE19854005wEngAbs.pdf	2380442 45e8cde2eaf14ce0f511355350cdaab29215b112	no	13
Warnings:					
Information:					
6	Foreign Reference	DE19854012A1wEngTrans.pdf	5627862 3db2a46017921dcd9a33d1365771806b74b598b5	no	31
Warnings:					
Information:					

7	Foreign Reference	DE4200639AwEngEquiv.pdf	2044063	no	16
			b6af3ec59b378147b239c522b4a454a298b01f56		
Warnings:					
Information:					
8	Foreign Reference	EP532194A1.pdf	1752602	no	27
			7918e253582f3e84a941157a255011e5a52ad383		
Warnings:					
Information:					
9	Foreign Reference	EP535695A2.pdf	1528587	no	23
			1aae768ef9cdba6f82365a69aee11d9341893eaf		
Warnings:					
Information:					
10	Foreign Reference	EP2325093B1.pdf	6029087	no	21
			e4bda6df145469ee627a657903e2e1628415d75a		
Warnings:					
Information:					
11	Foreign Reference	EP1458388A_WO2003055486A1.pdf	2313920	no	50
			be7924f9514571b38934858507bad76531ac4ce2		
Warnings:					
Information:					
12	Foreign Reference	EP2609821A1.pdf	4738067	no	16
			1e795909a4c5f33c844d8f0867da587de10fab0b		
Warnings:					
Information:					
13	Foreign Reference	ES2118034A1wEngAbs.pdf	1087511	no	8
			cc18daf1a8090becb3a1dcba33e4c1c5ab6368b1		
Warnings:					
Information:					
14	Foreign Reference	GB1025630A.pdf	239425	no	4
			2fc29ab8a0b705ec9fdcd323556b38781418221		
Warnings:					
Information:					
15	Foreign Reference	GB1065678A.pdf	375489	no	5
			aa2b606466521a51c334d29a9c96c37e87799b7a		
Warnings:					
Information:					

16	Foreign Reference	IE-S2005-0051.pdf	1382617	no	38
			ee0c2c341c7031de94494170c8af275559913822		
Warnings:					
Information:					
17	Foreign Reference	IE-S2005-0563.pdf	1242261	no	35
			39c7fbcc084566c319b6ef47671b30e307f75a8f		
Warnings:					
Information:					
18	Foreign Reference	IE-S2005-0615.pdf	687209	no	19
			e85220403c387543cc0d9938d04c6484f27be879		
Warnings:					
Information:					
19	Foreign Reference	JP02-145179AwEngEquiv.pdf	6424769	no	23
			7deb3c67a8d6443a1d468f9e6538b8b25b415549		
Warnings:					
Information:					
20	Foreign Reference	JP03-049671wEngEquiv.pdf	2425585	no	15
			933dfd59b7c1c4ad1a157dbef18204add1d2cc7f		
Warnings:					
Information:					
21	Foreign Reference	JP03-180166AwEngEquiv.pdf	9824634	no	39
			9938dcd386cd1f52a6bf76059cff070f1fcd384e		
Warnings:					
Information:					
22	Foreign Reference	JP09-075058AwEngAbs.pdf	1568690	no	6
			8ef4cfa3ddabb8f24b4c6300cbdc02790b8f84c1		
Warnings:					
Information:					
23	Foreign Reference	JP11-178563AwEngAbs.pdf	1813978	no	7
			e158df38786768234073d43a683b96f40f2f58dc		
Warnings:					
Information:					
24	Foreign Reference	CN102754924A_wMachTrans.pdf	3257682	no	22
			ca02f6467f1b7e914e4dd95137c1b133b13d2606		
Warnings:					
Information:					

25	Foreign Reference	CN1122213-1of2.pdf	22458294	no	24
			15d37d32f981dd64af5faa2fa5f20ea9336f2e5e		
Warnings:					
Information:					
26	Foreign Reference	CN1122213-2of2.pdf	20787363	no	24
			f15787bdfc541274bcb21dc3c54ccf94fa2c0b7		
Warnings:					
Information:					
27	Foreign Reference	JP2000203639wEngAbs.pdf	1225290	no	6
			d318244d68ad467d914f9d61e0af71438c421872		
Warnings:					
Information:					
28	Foreign Reference	JP2000236865wEngAbs.pdf	1502432	no	7
			550042330159239467a8a3df4f6c5edb27ae5b27		
Warnings:					
Information:					
29	Foreign Reference	JP2001165437AwEngAbs.pdf	1266359	no	9
			5c48b710b16d663f4a3f9e7ac2760fbc3636fb88		
Warnings:					
Information:					
30	Foreign Reference	JP2005034021AwEngCorres.pdf	5963090	no	31
			de609c9423784b94e4ec12f138be519a245f41e6		
Warnings:					
Information:					
31	Foreign Reference	JP2006504430AwEngEquiv.pdf	8899201	no	46
			c5cefa6c5b35ae4f3902e3b9791ef4f9b2c98610		
Warnings:					
Information:					
32	Foreign Reference	JP62-278975wEngAbs.pdf	89429	no	4
			a3958c78c9ef79ba2416dd2b0b28648f387e40af		
Warnings:					
Information:					
33	Foreign Reference	JP64-37276AwEngEquiv.pdf	14701377	no	47
			217e6d6d90e60e6db4a55731ca98af9220151ce1		
Warnings:					
Information:					

34	Foreign Reference	KR0193885BwEngEquiv.pdf	503187	no	26
			b3b004f21959fbc19fd34864c674274d6c7ac45		
Warnings:					
Information:					
35	Foreign Reference	WO1995001137A1.pdf	1735246	no	50
			7e1969447dce41955b61ff1feb51fbd089204796		
Warnings:					
Information:					
36	Foreign Reference	WO1997012639A1.pdf	2386843	no	57
			afc2e44a3f0435edfa166bc6e2924bd44b83f9da		
Warnings:					
Information:					
37	Foreign Reference	WO2000028842A1.pdf	1419312	no	29
			ff5fa0a352529a73010c8fda865841ae7d2b2a40		
Warnings:					
Information:					
38	Foreign Reference	WO2003056948A1.pdf	598077	no	16
			7d0854bf1b9cf9a489896a4260d10f80a518125c		
Warnings:					
Information:					
39	Foreign Reference	WO2003082031A1.pdf	1046764	no	22
			6c36955c46e0270026225f31d7160ac212923294		
Warnings:					
Information:					
40	Foreign Reference	WO2003094900A1.pdf	2267379	no	43
			26b6a795a00fe4d35560ba552482e3e8367ca72d		
Warnings:					
Information:					
41	Foreign Reference	WO2004064548A1.pdf	1366459	no	34
			3cfad380aa4713db1a2ca3732d9f259c338459be		
Warnings:					
Information:					
42	Foreign Reference	WO2005020726A1.pdf	1471936	no	31
			11b6a2fceb4b009c36f0571f3ba4a2dd04be41c4		
Warnings:					
Information:					

43	Foreign Reference	WO2006015070A1.pdf	865377	no	25
			fcd97015cf0f216eec074987ca3d54f2ee9d5400		
Warnings:					
Information:					
44	Foreign Reference	WO2007026131A1.pdf	3846883	no	62
			423e5b58a863e4e1f8f0a27092df1fe628b2a4ed		
Warnings:					
Information:					
45	Foreign Reference	WO2010023561A1.pdf	4656892	no	87
			8dcd8346589cb7256a5d2d310cefa8c7109978ed		
Warnings:					
Information:					
46	Foreign Reference	WO2011033396A2.pdf	905927	no	24
			4884fa26c6e0e115647ac311feda5503cfb2068		
Warnings:					
Information:					
47	Foreign Reference	WO2011117580A2.pdf	1210636	no	33
			d8b074ede89c37608af329b3aa48da1125cc8ae5		
Warnings:					
Information:					
48	Foreign Reference	WO2012021972A1.pdf	1443479	no	39
			6266c29e43a20c1a186c4f38d52197f05e2dd47f		
Warnings:					
Information:					
49	Foreign Reference	WO2012027350A2.pdf	1422461	no	33
			70dad7113fc0c0a75709cd5e1659a42d00a96d45		
Warnings:					
Information:					
50	Foreign Reference	WO2012085207A1.pdf	1468326	no	33
			45f68ac22a5a45ce44d3947d491020854c2aba99		
Warnings:					
Information:					
51	Foreign Reference	WO2013050934A1.pdf	1041561	no	22
			327ab2c64b6267fbb3811bcceb13e5c14540c6e3		
Warnings:					
Information:					

52	Foreign Reference	WO2013083635A1.pdf	1080754	no	24
			ad219e1bb2ee22d34eccbc92b68f879759a13abd		
Warnings:					
Information:					
53	Foreign Reference	WO2013098398A2.pdf	2124160	no	41
			914200bbbabb4d094ef50133d72bbf9231a9faf4a		
Warnings:					
Information:					
54	Foreign Reference	WO2013142678A1.pdf	633376	no	20
			69b823492ddb6f6bd698408463259b6cc4d9f089		
Warnings:					
Information:					
55	Foreign Reference	WO2014093127A2.pdf	3526985	no	64
			56d9259a7d2721eaa3d93225bf2ca4cc2912ebd8		
Warnings:					
Information:					
56	Foreign Reference	WO2014118286A2.pdf	5527272	no	102
			af9634f8d1ad7443e50da9ce1c2026409aec4531		
Warnings:					
Information:					
57	Foreign Reference	WO2014139611A1.pdf	1766996	no	30
			301366cbdcac72391f59ab8bf4fdff6c53ac0652d		
Warnings:					
Information:					
58	Foreign Reference	WO2014140087A1.pdf	1523215	no	33
			69a9579031094fcb44b70ea2deaff13a8f2267a		
Warnings:					
Information:					
59	Foreign Reference	WO2014187763A1.pdf	2710665	no	34
			53415c1ce02d6483d7f7f050b36f9e4f264b81b4		
Warnings:					
Information:					
60	Fee Worksheet (SB06)	fee-info.pdf	30801	no	2
			10341bc9585acc104b8d8a9c954175bb2687d26d		
Warnings:					
Information:					

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on 3-16-2016.Bryan Flick
Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
 First Named Inventor : Adam Bowen
 Filed : October 28, 2015
 Art Unit : 1747
 Examiner : Mayes, Dionne Walls
 Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
 AND METHODS THEREOF
 Customer No. : 66854

INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and /or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT

☐ **37 CFR §1.97(b)**

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ 1). Within 3 months of the application filing date, or
- ☐ 2). Within 3 months of entry of a national stage as set forth in § 1.491, or
- ☐ 3). Before the mail date of a first Office Action on the merits, or
 - ☐ 3a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
- ☐ 4). Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
 - ☐ 4a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☒ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☒ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☒ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☐ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☐ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under §1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement

--AND--

B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☒ **37 CFR §1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☒ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☒ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☒ **37 CFR §1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☒ 3). A copy of each application specification is not submitted because the application is stored in the IFW. Cite no(s): 484 and 485

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☒ **37 CFR §1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☒ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

- ☒ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**
- ☒ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☒ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**
- ☒ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☒ 2a). An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): 375-381, 390, 396-408, 411, 412, and 453
- AND/OR--**
- ☒ 2b). A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): 375, 376, 378, 380, 381, 396-398, 404, 405, 407, and 408
- OR--**
- ☐ 3). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

STATEMENT UNDER 37 CFR § 1.97(e)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. Cite no(s):
- ☐ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement. Cite no(s):

STATEMENT UNDER 37 CFR § 1.704(d)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

- ☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$180.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

Dated: 3/16/2014

By: 
Richard D. Shoop, Reg. No. 45,763

Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854



- (51) International Patent Classification:
A24F 47/00 (2006.01)
- (21) International Application Number:
PCT/EP2014/060225
- (22) International Filing Date:
19 May 2014 (19.05.2014)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
13168609.9 21 May 2013 (21.05.2013) EP
- (71) Applicant: PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).
- (72) Inventors: THORENS, Michel; Les Combremonts 24,
CH-1510 Moudon (CH). COCHAND, Olivier; Le Fau-
bourg 30, CH-2056 Dombresson (CH).
- (74) Agent: MILLBURN, Julie; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).
- (81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

- (84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

- without international search report and to be republished
upon receipt of that report (Rule 48.2(g))

(54) Title: ELECTRICALLY HEATED AEROSOL DELIVERY SYSTEM

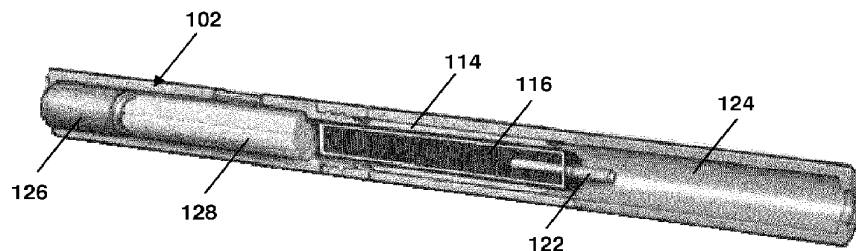


Figure 1(b)

(57) Abstract: The invention relates to an aerosol delivery system for delivering aerosolised medicament particles to a user comprising a cartridge and a device configured to receive the cartridge. The cartridge comprises: a first compartment comprising a delivery enhancing compound source; a second compartment comprising a medicament source; a vaporiser for heating the medicament; and a transfer element for conveying the medicament from the second compartment to the vaporiser. The cartridge may further comprise an aerosol forming chamber in fluid communication with the first compartment and the second compartment. The device comprises: an outer housing; a power source; temperature controlling means for controlling the temperature of the first compartment of the cartridge; and electronic circuitry configured to control power to the temperature controlling means from the power source. The electronic circuitry is configured to maintain the first compartment of the cartridge at a temperature of between about 30°C and about 50°C. In use, the medicament reacts with the delivery enhancing compound in the gas phase to form aerosolised medicament-containing particles.



ELECTRICALLY HEATED AEROSOL DELIVERY SYSTEM

The invention relates to a cartridge for an aerosol delivery system and to a device configured to receive the cartridge. The invention also relates to an aerosol delivery system for delivering aerosolised medicament, such as nicotine salt particles, to a user comprising a device and a cartridge, in particular to a smoking device for delivering aerosolised nicotine salt particles to a user. The invention further relates to a method of delivering aerosolised medicament, such as nicotine salt particles, to a user.

So-called 'e-cigarettes' and other electrically operated smoking systems that vaporise a liquid nicotine formulation to form an aerosol that is inhaled by a user are known in the art. For example, WO 2009/132793 A1 discloses an electrically heated smoking system comprising a shell and a replaceable mouthpiece wherein the shell comprises an electric power supply and electric circuitry. The mouthpiece comprises a liquid storage portion, a capillary wick having a first end that extends into the liquid storage portion for contact with liquid therein, and a heating element for heating a second end of the capillary wick. In use, liquid is transferred from the liquid storage portion towards the heating element by capillary action in the wick. Liquid at the second end of the wick is vaporised by the heating element. The liquid preferably comprises a tobacco-containing material comprising volatile tobacco flavour compounds which are released from the liquid upon heating.

Commercially available e-cigarettes typically require significant power in order to form an aerosol having suitable particle size for delivery to a user.

WO 2008/121610 A1 and WO 2011/034723 A1 disclose devices and methods for delivering nicotine or other medicaments to a subject in which pyruvic acid is reacted with nicotine or other medicaments in the gas phase to form an aerosol of nicotine, or medicament, pyruvate salt particles. At room temperature both pyruvic acid and nicotine are sufficiently volatile to form respective vapours that react with one another to form nicotine pyruvate salt particles. However, pyruvic acid has a greater vapour pressure than nicotine at a given temperature. As a result, the efficiency of the gas phase reaction between the pyruvic acid and the nicotine is highly dependent on the ambient temperature, which can disadvantageously lead to inconsistent nicotine delivery to a user.

It would be desirable to provide an aerosol delivery system that operates with reduced power consumption as compared to commercially available e-cigarettes. It would also be desirable to provide an aerosol delivery system that allows for more consistent nicotine or other medicament delivery per puff as compared to known devices for delivering aerosolised nicotine salt particles.

According to the invention, there is provided, a cartridge comprising: a first compartment comprising a volatile delivery enhancing compound source; a second

compartment comprising a medicament source; a vaporiser for heating the medicament; and a transfer element for conveying the medicament from the second compartment to the vaporiser.

As discussed further below, use of cartridges according to the invention in an aerosol delivery system advantageously allows for more consistent medicament delivery as compared to known devices for delivering aerosolised nicotine, or medicament, salt particles. That is to say, the medicament delivery per puff during use of cartridges according to the invention in an aerosol delivery system is more consistent, than in known devices for delivering aerosolised nicotine, or medicament, salt particles. Furthermore, the medicament delivery per puff during use of cartridges according to the invention in an aerosol delivery system is more constant than in known devices for delivering aerosolised nicotine, or medicament, salt particles.

As used herein, the term "volatile" refers to a delivery enhancing compound having a vapour pressure of at least about 20 Pa. Unless otherwise stated, all vapour pressures referred to herein are vapour pressures at 25°C measured in accordance with ASTM E1194 – 07.

Preferably, the volatile delivery enhancing compound has a vapour pressure of at least about 50 Pa, more preferably at least about 75 Pa, most preferably at least 100 Pa at 25°C.

Preferably, the volatile delivery enhancing compound has a vapour pressure of less than or equal to about 400 Pa, more preferably less than or equal to about 300 Pa, even more preferably less than or equal to about 275 Pa, most preferably less than or equal to about 250 Pa at 25°C.

In certain embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 20 Pa and about 400 Pa, more preferably between about 20 Pa and about 300 Pa, even more preferably between about 20 Pa and about 275 Pa, most preferably between about 20 Pa and about 250 Pa at 25°C.

In other embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 50 Pa and about 400 Pa, more preferably between about 50 Pa and about 300 Pa, even more preferably between about 50 Pa and about 275 Pa, most preferably between about 50 Pa and about 250 Pa at 25°C.

In further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 75 Pa and about 400 Pa, more preferably between about 75 Pa and about 300 Pa, even more preferably between about 75 Pa and about 275 Pa, most preferably between about 75 Pa and about 250 Pa at 25°C.

In yet further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 100 Pa and about 400 Pa, more preferably between about 100 Pa and about 300 Pa, even more preferably between about 100 Pa and about 275 Pa, most preferably between about 100 Pa and about 250 Pa at 25°C.

The volatile delivery enhancing compound may comprise a single compound. Alternatively, the volatile delivery enhancing compound may comprise two or more different compounds.

Where the volatile delivery enhancing compound comprises two or more different compounds, the two or more different compounds in combination have a vapour pressure of at least about 20 Pa at 25°C.

Preferably, the volatile delivery enhancing compound is a volatile liquid.

The volatile delivery enhancing compound may comprise a mixture of two or more different liquid compounds.

The volatile delivery enhancing compound may comprise an aqueous solution of one or more compounds. Alternatively the volatile delivery enhancing compound may comprise a non-aqueous solution of one or more compounds.

The volatile delivery enhancing compound may comprise two or more different volatile compounds. For example, the volatile delivery enhancing compound may comprise a mixture of two or more different volatile liquid compounds.

Alternatively, the volatile delivery enhancing compound may comprise one or more non-volatile compounds and one or more volatile compounds. For example, the volatile delivery enhancing compound may comprise a solution of one or more non-volatile compounds in a volatile solvent or a mixture of one or more non-volatile liquid compounds and one or more volatile liquid compounds.

In one embodiment, the volatile delivery enhancing compound comprises an acid. The volatile delivery enhancing compound may comprise an organic acid or an inorganic acid. Preferably, the volatile delivery enhancing compound comprises an organic acid, more preferably a carboxylic acid, most preferably an alpha-keto or 2-oxo acid.

In a preferred embodiment, the volatile delivery enhancing compound in the first compartment comprises an acid selected from the group consisting of 3-methyl-2-oxovaleric acid, pyruvic acid, 2-oxovaleric acid, 4-methyl-2-oxovaleric acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof. In a particularly preferred embodiment, the first compartment comprises pyruvic acid.

In one embodiment, the volatile delivery enhancing compound comprises ammonium chloride.

In a preferred embodiment, the volatile delivery enhancing compound source comprises a sorption element and a volatile delivery enhancing compound sorbed on the sorption element.

As used herein, by "sorbed" it is meant that the volatile delivery enhancing compound is adsorbed on the surface of the sorption element, or absorbed in the sorption element, or both adsorbed on and absorbed in the sorption element. Preferably, the volatile delivery enhancing compound is adsorbed on the sorption element.

The sorption element may be formed from any suitable material or combination of materials. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded
5 polytetrafluoroethylene (ePTFE), and BAREX®.

In a preferred embodiment, the sorption element is a porous sorption element.

For example, the sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

10 The sorption element is preferably chemically inert with respect to the volatile delivery enhancing compound.

The sorption element may have any suitable size and shape.

In one preferred embodiment, the sorption element is a substantially cylindrical plug. In one particularly preferred embodiment, the sorption element is a porous substantially cylindrical
15 plug.

In another preferred embodiment, the sorption element is a substantially cylindrical hollow tube. In another particularly preferred embodiment, the sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the sorption element may be chosen to allow a
20 desired amount of volatile delivery enhancing compound to be sorbed on the sorption element.

In a preferred embodiment, between about 20 µl and about 200 µl, more preferably between about 40 µl and about 150 µl, most preferably between about 50 µl and about 100 µl of the volatile delivery enhancing compound is sorbed on the sorption element.

The sorption element advantageously acts as a reservoir for the volatile delivery
25 enhancing compound.

The adsorption element may be configured to convey the volatile delivery enhancing compound from within the first compartment into air drawn through the cartridge. For example, the adsorption element may comprise a capillary material for conveying the volatile delivery enhancing compound from the first compartment into air drawn through the cartridge by
30 capillary action. In certain embodiments, the adsorption element may comprise a capillary wick for conveying the volatile delivery enhancing compound from the first compartment into air drawn through the cartridge by capillary action.

The use of a volatile delivery enhancing compound advantageously allows aerosol delivery systems comprising cartridges according to the invention to operate with reduced
35 power consumption as compared to commercially available e-cigarettes. The power consumption of the aerosol delivery system can be reduced by reducing the power required to vaporise the medicament because the volatile delivery enhancing compound increases the

delivery rate of medicament to a user. In contrast, in commercially available e-cigarettes in order to increase the delivery rate of nicotine to a user, additional power is required to vaporise the nicotine formulation to generate smaller aerosol particles. By reducing the power required to generate a suitable aerosol for delivery to a user, the operating temperature of aerosol delivery systems comprising cartridges according to the invention may also be advantageously reduced.

In this way, the invention allows a cost effective, compact and easy to use aerosol delivery system to be provided. Furthermore, by using an acid or ammonium chloride as a delivery enhancing compound in cartridges according to the invention, the pharmacokinetic rate of the medicament as compared to commercially available e-cigarettes may be advantageously increased.

In a preferred embodiment, the cartridge further comprises an aerosol forming chamber in fluid communication with the first compartment and the second compartment. In use, the medicament reacts with the volatile delivery enhancing compound in the gas phase in the aerosol forming chamber to form aerosolised medicament-containing particles.

Preferably, the cartridge further comprises at least one air inlet upstream of the first compartment, and at least one air outlet downstream of the aerosol forming chamber, the at least one air inlet and the at least one air outlet being arranged to define an air flow pathway extending from the at least one air inlet to the at least one air outlet via the first compartment, the vaporiser and the aerosol forming chamber.

As used herein, the terms "upstream" and "downstream" are used to describe the relative positions of components, or portions of components, of cartridges, aerosol delivery devices and aerosol delivery systems according to the invention in relation to the direction of air drawn through the cartridges, aerosol delivery devices and aerosol delivery systems during use thereof.

As used herein, the term "air inlet" is used to describe one or more apertures through which air may be drawn into the cartridge.

As used herein, the term "air outlet" is used to describe one or more apertures through which air may be drawn out of the cartridge.

In a preferred embodiment, the at least one air inlet comprises a plurality of perforations provided in an outer housing of the cartridge. Preferably the perforations extend circumferentially around the outer housing.

Preferably, the medicament has a melting point below about 150 degrees Celsius.

Alternatively or in addition, preferably the medicament has a boiling point below about 300 degrees Celsius.

In certain preferred embodiments, the medicament comprises one or more aliphatic or aromatic, saturated or unsaturated nitrogenous bases (nitrogen containing alkaline compounds) in which a nitrogen atom is present in a heterocyclic ring or in an acyclic chain (substitution).

The medicament may comprise one or more compounds selected from the group consisting of: nicotine; 7-Hydroxymitragynine; Arecoline; Atropine; Bupropion; Cathine (D-norpseudoephedrine); Chlorpheniramine; Dibucaine; Dimemorphan, Dimethyltryptamine, Diphenhydramine, Ephedrine, Hordenine, Hyoscyamine, Isoarecoline, Levorphanol, Lobeline, Mesembrine, Mitragynine, Muscatine, Procaine, Pseudo ephedrine, Pylamine, Raclopride, Ritodrine, Scopolamine, Sparteine (Lupinidine) and Ticlopidine; tobacco smoke constituents, such as 1,2,3,4 Tetrahydroisoquinolines, Anabasine, Anatabine, Cotinine, Myosmine, Nicotrine, Norcotinine, and Nornicotine; anti-asthmatic drugs, such as Orciprenaline, Propranolol and Terbutaline; anti-angina drugs, such as Nicorandil, Oxprenolol and Verapamil; antiarrhythmic drugs, such as Lidocaine; nicotinic agonists, such as Epibatidine, 5-(2R)-azetidylmethoxy)-2-chloropyridine (ABT-594), (S)-3-methyl-5-(1-methyl-2-pyrrolidinyl)isoxazole (ABT 418) and ($\pm$)-2-(3-Pyridinyl)-1-azabicyclo[2.2.2]octane (RJR-2429); nicotinic antagonists, such as Methyllycacinine and Mecamylamine; acetyl cholinesterase inhibitors, such as Galantamine, Pyridostigmine, Physostigmine and Tacrine; and MAO-inhibitors, such as Methoxy-N,N-dimethyltryptamine, 5-methoxy- α -methyltryptamine, Alpha-methyltryptamine, Iproclozide, Iproniazide, Isocarboxazide, Linezolid, Meclobemide, N,N- Dimethyltryptamine, Phenelzine, Phenyl ethylamine, Toloxatone, Tranylcypromine and Tryptamine.

The medicament source is preferably a nicotine source.

The medicament source may comprise a sorption element and a medicament sorbed on the sorption element.

The second compartment may comprise a sorption element with a medicament sorbed thereon. More preferably, the second compartment comprises a porous sorption element with the medicament sorbed thereon. The porous sorption element may comprise one or more porous materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres. The one or more porous materials may or may not be capillary materials and are preferably inert with respect to the medicament. The particular preferred porous material or materials will depend on the physical properties of the medicament. The one or more porous materials may have any suitable porosity so as to be used with different medicaments having different physical properties.

Inclusion of a sorption element with a medicament sorbed thereon in the second compartment may advantageously reduce the risk of leakage of the medicament from the cartridge.

Furthermore, by choosing a sorption element having suitable properties, the inclusion of a sorption element may allow improved control of the release of the medicament.

In preferred embodiments, the first compartment of the cartridge comprises a volatile delivery enhancing compound source and the second compartment of the cartridge comprises a nicotine source. The nicotine source may comprise one or more of nicotine, nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate, or a nicotine derivative.

The nicotine source may comprise natural nicotine or synthetic nicotine.

The nicotine source may comprise pure nicotine, a solution of nicotine in an aqueous or non-aqueous solvent or a liquid tobacco extract.

The nicotine source may further comprise an electrolyte forming compound. The electrolyte forming compound may be selected from the group consisting of alkali metal hydroxides, alkali metal oxides, alkali metal salts, alkaline earth metal oxides, alkaline earth metal hydroxides and combinations thereof.

For example, the nicotine source may comprise an electrolyte forming compound selected from the group consisting of potassium hydroxide, sodium hydroxide, lithium oxide, barium oxide, potassium chloride, sodium chloride, sodium carbonate, sodium citrate, ammonium sulfate and combinations thereof.

In certain embodiments, the nicotine source may comprise an aqueous solution of nicotine, nicotine base, a nicotine salt or a nicotine derivative and an electrolyte forming compound.

Alternatively or in addition, the nicotine source may further comprise other components including, but not limited to, natural flavours, artificial flavours and antioxidants. Preferably, the second compartment comprises a liquid medicament source. Preferably, the second compartment is configured to hold between about 50 microlitres and about 150 microlitres of the liquid medicament, more preferably about 100 microlitres of the liquid medicament.

The liquid medicament has a boiling point suitable for use in an aerosol delivery system as described herein: if the boiling point is too high, the vaporiser will not be able to vaporise the liquid medicament. The liquid medicament also has physical properties that allow the medicament to be conveyed by the transfer element from the second compartment to the vaporiser. Preferably, the liquid medicament has physical properties, including viscosity, that allow the liquid medicament to be conveyed through the transfer element from the second compartment to the vaporiser by capillary action.

The vaporiser is preferably located downstream of the first compartment such that air drawn through the cartridge passes through the first compartment before passing over the vaporiser.

The vaporiser preferably comprises an electrically operated heater, the heater being connectable to an electric power supply. The heater preferably comprises at least one heating element configured to heat the medicament to form a medicament-containing vapour. The

heater may comprise a single heating element. Alternatively, the heater may comprise more than one heating element, for example two, three, four, five, six or more heating elements. The heating element or heating elements may be arranged appropriately so as to most effectively vaporise the medicament. The cartridge preferably comprises electrical contacts configured to be coupled to a power source in an aerosol delivery device for providing power to the at least one heating element.

The at least one heating element preferably comprises an electrically resistive material. Suitable electrically resistive materials include but are not limited to: semiconductors such as doped ceramics, electrically 'conductive' ceramics (such as, for example, molybdenum disilicide), carbon, graphite, metals, metal alloys and composite materials made of a ceramic material and a metallic material. Such composite materials may comprise doped or undoped ceramics. Examples of suitable doped ceramics include doped silicon carbides. Examples of suitable metals include titanium, zirconium, tantalum and metals from the platinum group. Examples of suitable metal alloys include stainless steel, nickel-, cobalt-, chromium-, aluminium-titanium- zirconium-, hafnium-, niobium-, molybdenum-, tantalum-, tungsten-, tin-, gallium-, manganese- and iron-containing alloys, and super-alloys based on nickel, iron, cobalt, stainless steel, Timetal and iron-manganese-aluminium based alloys. In composite materials, the electrically resistive material may optionally be embedded in, encapsulated or coated with an insulating material or vice-versa, depending on the kinetics of energy transfer and the external physicochemical properties required. Examples of suitable composite heating elements are disclosed in US 5,498,855, WO 03/095688 A2 and US 5,514,630.

The at least one heating element may take any suitable form. For example, the at least one heating element may take the form of a heating blade, such as those described in US 5,388,594, US 5,591,368 and US 5,505,214. Alternatively, the at least one heating element may take the form of a casing or substrate having different electro-conductive portions, as described in EP 1 128 741 A1, or an electrically resistive metallic tube, as described in WO 2007/066374 A1. Alternatively, the at least one heating element may be a disk (end) heater or a combination of a disk heater with heating needles or rods. Alternatively, the at least one heating element may take the form of a metallic etched foil insulated between two layers of an inert material. In such embodiments, the inert material may comprise Kapton®, all-polyimide or mica foil. Alternatively, the at least one heating element may take the form of a sheet of material, which may be rolled around the vaporiser. The sheet may be made from any suitable material, for example an iron-aluminium based alloy, an iron-manganese-aluminium base alloy or Timetal. The sheet may be rectangular in shape, or may have a patterned shape which may form a coil-like structure when rolled around the vaporiser. Other alternatives include a heating wire or filament, for example a Ni-Cr, platinum, tungsten or alloy wire, such as those described in EP 1 736 065 A1, or a heating plate.

In a preferred embodiment, the at least one heating element comprises a coil of wire surrounding the vaporiser. In that embodiment, preferably the wire is a metal wire. Even more preferably, the wire is a metal alloy wire. The heating element may completely or partially encircle the vaporiser.

5 In an alternative embodiment, the vaporiser may comprise an atomiser including the at least one heating element. In addition to the heating element, the atomiser may include one or more electromechanical elements such as piezoelectric elements. Additionally or alternatively, the atomiser may also include elements that use electrostatic, electromagnetic or pneumatic effects.

10 The transfer element may comprise a porous material. The transfer element may have a first portion, which extends into the second compartment, and a second portion adjacent to the vaporiser.

15 Preferably, the transfer element comprises a capillary material for conveying the medicament from the second compartment to the vaporiser by capillary action. The capillary material may be a capillary wick having a first portion, which extends into the second compartment, and a second portion adjacent to the vaporiser. In use, the medicament is transferred from the second compartment to the vaporiser by capillary action in the capillary wick. When the vaporiser is activated, the medicament in the second portion of the capillary wick is vaporised to form a medicament-containing vapour.

20 Preferably, the vaporiser is configured to heat the medicament in the second portion of the capillary wick to a temperature of between about 60°C and about 150°C. More preferably, the vaporiser is configured to heat the medicament in the second portion of the capillary wick to a temperature of between about 65°C and about 120°C. Yet more preferably, the vaporiser is configured to heat the medicament in the second portion of the capillary wick to a temperature
25 of between about 70°C and about 100°C to form a medicament-containing vapour.

The capillary wick may be a linear capillary wick having a first free end extending into the second compartment and a second free end adjacent to the vaporiser. Alternatively, the capillary wick may be a convoluted capillary wick. In such embodiments, the first portion of the capillary wick extending into the vaporiser and the second portion of the capillary wick adjacent
30 to the vaporiser may be free ends of the capillary wick or convoluted portions of the capillary wick. For example, the capillary wick may be a U-shaped capillary wick wherein the curved portion of the U-shaped capillary wick extends into the second compartment and the free ends of the U-shaped capillary wick are adjacent to the vaporiser. Alternatively, the capillary wick may be a U-shaped capillary wick wherein the free ends of the U-shaped capillary wick extend
35 into the second compartment and the curved portion of the U-shaped capillary wick is adjacent to the vaporiser. It will be appreciated that any other suitable shape of capillary wick may also be used.

The capillary wick may have a fibrous or spongy structure. For example, the capillary wick may comprise a plurality of fibres or threads, generally aligned in the longitudinal direction of the cartridge, or sponge-like material formed into a rod shape along the longitudinal direction of the cartridge. The structure of the wick forms a plurality of small bores or tubes, through which the medicament can be transported from the second compartment to the vaporiser, by capillary action. The capillary wick may comprise any suitable material or combination of materials. Examples of suitable materials are ceramic- or graphite-based materials in the form of fibres or sintered powders. The capillary wick may have any suitable capillarity and porosity so as to be used with medicaments having different physical properties such as density, viscosity, surface tension and vapour pressure.

A porous material may be provided between the capillary wick and the vaporiser. The porous material may be any suitable material that is permeable to the medicament and allows the medicament to migrate from the capillary wick to the vaporiser. The porous material is preferably inert with respect to the medicament. The porous material may or may not be a capillary material. The porous material may comprise a hydrophilic material to improve distribution and spread of the medicament. This may assist with consistent vapour formation. The particular preferred material or materials will depend on the physical properties of the medicament. The porous material may have any suitable porosity so as to be used with medicaments having different physical properties. Preferably, the capillary wick and the porous material are in contact, as this provides for good transfer of the medicament.

The at least one heating element may heat the medicament at the second end of the capillary wick by means of conduction. The heating element may be at least partially in contact with the second end of the capillary wick. Alternatively, heat from the heating element may be conducted to the medicament at the second end of the capillary wick by means of a heat conductive element. Alternatively, the at least one heating element may transfer heat to ambient air drawn through the cartridge during use, which in turn heats the medicament at the second end of the capillary wick by convection. The ambient air may be heated before passing over the second end of the capillary wick. Alternatively, the ambient air may be first drawn over the second end of the wick and then heated, as described in WO 2007/078273 A1.

The first compartment comprising the volatile delivery enhancing compound may be provided circumferentially around at least a portion of the second compartment. In such embodiments, the first compartment may be defined by an outer wall of the second compartment and an outer housing of the cartridge. Alternatively, the first compartment and the second compartment may be arranged sequentially along the longitudinal direction of the cartridge with the first compartment upstream from the second compartment. In such embodiments, the first compartment and the second compartment may abut one another or may be spaced apart along the longitudinal direction of the cartridge.

Preferably, the first compartment is substantially sealed prior to first use of the cartridge. For example, the first compartment may comprise one or more seals that may be punctured, or otherwise opened on first use of the cartridge.

As described above, the volatile delivery enhancing compound interacts with the medicament in the gas phase to form medicament-containing particles. Where the volatile delivery enhancing compound is an acid, and the medicament source is a nicotine source, the acid interacts with the nicotine in the gas phase to form nicotine salt particles. Preferably, the Mass Median Aerodynamic Diameter of the nicotine salt particles is less than about 6 microns. The Mass Median Aerodynamic Diameter of the nicotine salt particles may be less than about 1 micron. Preferably, the Mass Median Aerodynamic Diameter of the nicotine salt particles is between about 0.5 microns and about 5 microns.

The cartridge may further comprise a third compartment. Preferably, the third compartment is downstream of the second compartment. Where the cartridge comprises an aerosol forming chamber, the third compartment is preferably downstream of the aerosol forming chamber. The third compartment may comprise a flavour source. Alternatively or in addition, the third component may comprise a filtration material capable of removing at least a portion of any unreacted volatile delivery enhancing compound mixed with aerosolised medicament-containing particles drawn through the third compartment. The filtration material may comprise an adsorbent, such as activated carbon. As will be appreciated, any number of additional compartments may be provided as desired. For example, the cartridge may comprise a third compartment comprising a filter material and a fourth compartment downstream of the third compartment comprising a flavour source.

Preferably, the cartridge comprises an opaque outer housing. This advantageously reduces the risk of degradation of the volatile delivery enhancing compound and medicament due to exposure to light.

According to a further aspect of the invention, there is provided a device configured to receive a cartridge as described herein. The device comprises: an outer housing; a power source; temperature controlling means for controlling the temperature of the first compartment of the cartridge; and electronic circuitry configured to control power to the controlling means from the power source; wherein, the electronic circuitry is configured to maintain the first compartment of the cartridge at a temperature of between about 30°C and about 50°C.

In a preferred embodiment, the controlling means comprises a heater for heating the first compartment of the cartridge.

The use of such a device in combination with a cartridge according to the invention, advantageously allows for more consistent aerosol generation and medicament delivery per puff. By configuring the device to maintain the first compartment of the cartridge at a

temperature of between about 30°C and about 50°C, the effect of environmental conditions on aerosol generation and medicament delivery per puff can be mitigated.

Alternatively or in addition, the device may comprise a heater for heating ambient air drawn through the device to a temperature of between about 30°C and about 50°C before it passes through the first compartment of the cartridge.

According to a yet further aspect of the invention, there is provided an aerosol delivery system. The aerosol delivery system comprises: a device as described herein in cooperation with a cartridge as described herein. The device or cartridge comprises a first compartment comprising a volatile delivery enhancing compound. The device or cartridge comprises a second compartment comprising a medicament source. The device or cartridge comprises a vaporiser for heating the medicament. The device or cartridge further comprises a transfer element for conveying the medicament from the second compartment to the vaporiser. The device or cartridge further comprises an aerosol forming chamber in fluid communication with the first compartment and the second compartment. In use, the medicament reacts with the volatile delivery enhancing compound in the gas phase in the aerosol forming chamber to form aerosolised medicament-containing particles.

Preferably, the device or the cartridge further comprises a mouthpiece in fluid communication with the aerosol forming chamber. Preferably, the mouthpiece is part of the cartridge.

The mouthpiece may comprise any suitable material or combination of materials. Examples of suitable materials include thermoplastics that are suitable for food or pharmaceutical applications, for example polypropylene, polyetheretherketone (PEEK) and polyethylene.

Preferably, the cartridge is not refillable. Thus, when the medicament in the second compartment of the cartridge has been used up, the cartridge is replaced.

In certain embodiments, the device as well as the cartridge may be disposable.

Advantageously, all elements of the device which are potentially in contact with the volatile delivery enhancing compound or the medicament are changed when the cartridge is replaced. This avoids any cross-contamination in the device between different mouthpieces and different cartridges, for example cartridges comprising different volatile delivery enhancing compounds or medicaments.

The medicament in the second compartment may be advantageously protected from exposure to oxygen (because oxygen cannot generally enter the second compartment via the capillary wick or other transfer element) and in some embodiments light, so that the risk of degradation of the medicament is significantly reduced. Therefore, a high level of hygiene can be maintained. Also, the risk of the vaporiser becoming clogged with the medicament may be advantageously significantly reduced by replacing the cartridge at suitable intervals.

In preferred embodiments, the vaporiser comprises an electrically operated heater, the heater being connectable to the power source in the device. When the device and the cartridge are engaged, the heater in the cartridge is in electrical connection with the power supply via the circuitry, the circuitry is arranged to provide power to the heater in the cartridge. In one embodiment, power is provided to the heater in the cartridge when the user activates a switch. In this embodiment, the heater in the cartridge is then provided with substantially continuous power for a fixed period of time. Preferably, the power source has sufficient power to provide power to the heater in the cartridge for at least about 4 minutes, preferably at least about 5 minutes, and more preferably about 6 minutes. It has been found that the average duration of a smoking experience is approximately 6 minutes.

Preferably, the power source comprises sufficient power to enable the user to initiate between about 200 puffs and about 500 puffs.

In an alternative embodiment, power is provided to the heater in the cartridge only when a user initiates a puff. Preferably, the electric circuitry comprises a sensor to detect air flow indicative of a user taking a puff. The sensor may be an electro-mechanical device. Alternatively, the sensor may be any one of: a mechanical device, an optical device, an opto-mechanical device and a micro electro mechanical systems (MEMS) based sensor. In such embodiments, the electronic circuitry is preferably arranged to provide an electric current pulse to the heater in the cartridge when the sensor senses a user taking a puff. Preferably, the time-period of the electric current pulse is pre-set, depending on the amount of nicotine formulation desired to be vaporised. The electronic circuitry is preferably programmable for this purpose.

Alternatively, the electronic circuitry may comprise a manually operable switch for a user to initiate a puff. In such embodiments, the time-period of the electric current pulse sent to the heater in the cartridge upon manual operation of the switch by a user is preferably pre-set depending on the amount of nicotine formulation desired to be vaporised. The electronic circuitry is preferably programmable for this purpose.

Preferably, the power source comprises a cell contained in the device. The power source may be a Lithium-ion battery or one of its variants, for example a Lithium-ion polymer battery. Alternatively, the power source may be a Nickel-metal hydride battery or a Nickel cadmium battery or a fuel cell.

The power source may comprise circuitry chargeable by an external charging portion. In that case, preferably the circuitry, when charged, provides power for a pre-determined number of puffs, after which the circuitry must be re-connected to the external charging portion. An example of suitable circuitry is one or more capacitors or rechargeable batteries.

Preferably, the device and cartridge are arranged to releasably lock together when engaged.

The outer housing of the device may be formed from any suitable material or combination of materials. Examples of suitable materials include, but are not limited to, metals, alloys, plastics or composite materials containing one or more of those materials. Preferably, the outer housing is light and non-brittle.

5 The aerosol delivery system and device are preferably portable. The system aerosol delivery system may have a size and shape comparable to a conventional smoking article, such as a cigar or cigarette.

 According to a yet further aspect of the invention, there is provided a method of delivering aerosolised medicament-containing particles to a user. The method comprises:
10 controlling the temperature of a volatile delivery enhancing compound to between about 30°C and about 50°C to form a delivery enhancing compound- containing vapour; heating a medicament source to a temperature of between about 70°C and about 100°C form a medicament-containing vapour; and contacting the delivery enhancing compound-containing vapour with the medicament-containing vapour to form aerosolised medicament-containing
15 particles.

 In a preferred embodiment, the step of controlling the temperature of the delivery enhancing compound may include heating the delivery enhancing compound.

 As will be appreciated, a number of factors influence the formation of the medicament-containing particles. In general, in order to control the medicament delivery it is important to
20 control the vaporisation of the medicament and the volatile delivery enhancing compound. It is also important to control the relative quantities of the medicament and the volatile delivery enhancing compound. In the preferred embodiment, where the volatile delivery enhancing compound is an acid and the medicament source is a nicotine source, the molar ratio of acid to nicotine in the aerosol forming chamber is about 1:1. The use of acid or ammonium chloride as
25 a delivery enhancing compound has been found to approximately double the delivery rate of nicotine to a user for equivalent power supplied to the vaporiser.

 The vaporisation of the volatile delivery enhancing compound is controlled by the concentration of the volatile delivery enhancing compound in the first compartment, and by the exchange surface area of volatile delivery enhancing compound in the first compartment. The
30 vaporisation of the volatile delivery enhancing compound may be controlled by heating the first compartment of the cartridge or by heating ambient air drawn through the device before it passes through the first compartment of the cartridge. In preferred embodiments where the first compartment comprises pyruvic acid, preferably about 60 micrograms of pyruvic acid is vaporised per puff.

35 The vaporisation of the medicament may be controlled through the power supplied to the vaporiser and through the properties of the transfer element for conveying the medicament to the vaporiser.

Preferably, wherein the medicament source is a nicotine source, the power supplied to the vaporiser is between about 0.1 W and about 0.2 W in order to produce an optimal nicotine delivery to the user of about 100 micrograms per puff. More preferably, the power supplied to the heater is between about 0.13 W and about 0.14 W.

5 In commercial e-cigarettes, the power supplied to the vaporiser is generally much higher; in some cases measurements show a power supply of between about 3.7 W and about 5 W. The reduction in power consumption in aerosol delivery systems and devices according to the invention compared to such e-cigarettes is therefore significant. In addition, the operating temperature of the vaporiser in aerosol delivery systems and cartridges according to the invention can be reduced to between about 80°C to about 100°C compared to between about 200°C to about 300°C in commercial e-cigarettes.

For the avoidance of doubt, features described above in relation to one aspect of the invention may also be applicable to other aspects of the invention. In particular, features described above in relation to cartridges, devices and aerosol delivery systems according to the invention may also relate, where appropriate to methods according to the invention, and vice versa.

An exemplary embodiment of the invention will now be described with reference to the accompanying drawings in which:

Figures 1(a)-(d) show an embodiment of an aerosol delivery system according to the invention; and

Figure 2 shows a detailed view of a cartridge according to an embodiment of the invention without the outer housing.

Figure 1(a) shows an aerosol delivery system 100 having the approximate size and shape of a conventional smoking article, such as a cigar or cigarette. The aerosol delivery system 100 comprises a device 102, a cartridge 104 and a mouthpiece 106. The mouthpiece 106 forms part of the cartridge 104. The cartridge 104 comprises air inlets 108 positioned upstream of the mouthpiece, and an air outlet 110 at the mouth-end of the mouthpiece 106. A switch 112 is provided on the device.

Figure 1(b) shows a cross-sectional view of the aerosol delivery system 100, in which further detail of the device 102 and the cartridge 104 is shown. The cartridge 104 comprises a first compartment 114 comprising pyruvic acid and a second compartment 116 comprising a liquid nicotine formulation. As shown in Figure 1(b), the first compartment 114 is disposed circumferentially around the second compartment 116 and is defined by the outer circumferential surface of the second compartment 116 and the inner circumferential surface of the outer housing 118 of the cartridge 104.

As shown in Figure 1(c), the first compartment 114 comprises a porous plug of fibrous material 120 having pyruvic acid adsorbed thereon. The cartridge 104 further comprises a

capillary wick 122 having a first end inside the second compartment 116 and a second end outside the second compartment. The capillary wick 122 is configured to convey the liquid nicotine formulation from the second compartment 116 to a vaporiser surrounding the second end of the capillary wick 122. The vaporiser comprises an electric heater. An aerosol forming chamber 124 is provided downstream of the second compartment 116 in the mouthpiece 106. The mouthpiece 106 may comprise a third compartment (not shown) comprising a filtration material.

The device 102 comprises a power source 126 in the form of a rechargeable battery. The device 102 further comprises electronic circuitry 128 configured to control the supply of power from the power source 126 to the vaporiser. The device 102 also further comprises a heater (not shown) configured to heat the first compartment 114 of the cartridge 104.

Figure 1(c) shows the aerosol delivery system 100 with its component parts separated. The aerosol delivery system 100 is configured such that the cartridge 104 is disposable, and as such may be separated from the device 102, and replaced. A coupling portion 130 is provided to enable the cartridge 104 to be coupled to the device 102. The coupling portion 130 comprises a male threaded portion on the device 102 and a female threaded portion on the cartridge 104. The coupling portion 130 also comprises electrical connectors (not shown) that enable power to be provided to the vaporiser. Figure 1(d) shows an alternative view of the aerosol delivery system shown in Figure 1(c).

In use, a user puffs on the mouth-end of the mouthpiece 106, such that air is drawn into the cartridge 104 through the air inlets 108 in the outer housing 118, downstream through the cartridge 104, and then out of the air outlet 110 in the mouthpiece 106 into the user's mouth. The air enters the first compartment 114 and captures a vapour of the pyruvic acid by passing over the porous plug of fibrous material 120 having pyruvic acid adsorbed thereon. To enable consistent pyruvic acid vapour generation, the first compartment is heated by the heater in the device to approximately 40°C. Alternatively, the heater may heat the air drawn into the cartridge 104 through the air inlets 108 in the outer housing 118 before it passes through the first compartment 114. The air stream that exits the first compartment 114 and subsequently passes over the vaporiser is a pyruvic acid-containing air stream.

Puff detection sensors are provided (not shown) that communicate with the electronic circuitry 28. When a puff is sensed, the electronic circuitry activates the vaporiser to vaporise the liquid nicotine formulation. The pyruvic acid-containing air stream and the vaporised nicotine formulation are drawn downstream into the aerosol forming chamber 124. The pyruvic acid and the nicotine interact in the gas phase in the aerosol forming chamber 124 to form nicotine salt particles having a mass median aerodynamic particle diameter of between about 0.5 microns and about 5 microns. The aerosolised nicotine salt particles are drawn out of the cartridge 104 into the mouth of the user through the air outlet 110 in the mouthpiece 106. The

aerosol delivery system 100 is configured to deliver approximately 100 micrograms of nicotine to the user per puff. The electronic circuitry is configured to provide approximately 0.14 W of power to the vaporiser for each puff.

Any unreacted pyruvic acid can be removed from the nicotine salt particle aerosol by the filtration material in the third compartment in the mouthpiece 106.

The first compartment 116 is configured to hold approximately 150 microlitres of pyruvic acid, and the second compartment is configured to hold approximately 100 microlitres of the liquid nicotine formulation. The power source 126 is provided with sufficient power to enable approximately 200 to 500 puffs before it is required to be recharged. The volume of the first and second compartments is sufficient to also enable 200 to 500 puffs before the cartridge is required to be replaced. Each puff releases approximately 100 micrograms of nicotine and approximately 60 micrograms of pyruvic acid. In order to optimise the interaction between the nicotine and the pyruvic acid a molar ratio of approximately 1:1 is preferred.

Figure 2 shows a detailed view of a cartridge 200 comprising the first compartment and second compartment; the configuration shown is an alternative embodiment to that shown in Figures 1(a)-(d). For simplicity, the outer housing of the cartridge has been omitted from Figure 2. Figure 2 also shows the airflow pathway through the cartridge. As can be seen, the cartridge 200 comprises a first compartment 202 circumferentially surrounding a portion of the second compartment 116. The second end of the capillary wick 204 is circumscribed by an electric heater 206. The electric heater 206 is in the form of an elongate wire coiled around the capillary wick 204. The arrow 208 shows the airflow pathway from the air inlets through the first compartment 202, and over the capillary wick 204. Electrical contacts 210 are provided to connect the electric heater 206 to the power source in the device (not shown).

Nicotine discontinuous heating example

In order to avoid nicotine losses between puffs, and to simulate a puff detection system, a reference Health Canada smoking regime was applied (puff volume of 55 ml, puff duration of 2 seconds, 30 second interval between puffs) and the signal of the PDSP pump was used to drive the nicotine heating/ vaporization through a power supply unit during the 2s puffs.

In the following experiment, an aerosol delivery system shown in Fig 1b was prepared. A cartridge including a capillary wick and a heating wire was filled with pure nicotine, while a porous plug (Porex XMF-0507) saturated with 150 μ l pyruvic acid was positioned upstream in the puff airflow. Five smoking runs of 30 puffs were completed using increasing heating power from 0 to 0.2W. Deliveries from the groups of 30 puffs were collected on Cambridge filters and analyzed for Nicotine and Pyruvic acid. Results are presented in the table below:

Heating Power - W	$\mu\text{mol /puff}$	
	Nicotine	Pyruvic acid
0	0	0.28
0.05	0.02	0.21
0.1	0.18	0.22
0.15	0.62	0.36
0.2	0.94	0.35

As the pyruvic acid plug is not heated (kept at laboratory temperature of 22°C), the pyruvic acid deliveries are relatively constant, while the nicotine deliveries are increasing as a function of the heating power. In the configuration of the experiment, the optimal equimolar ratio is achieved when nicotine is heated between 0.1W and 0.15W.

The experiment confirms that the very low power heating requirement (compared to conventional e-cigarettes) provides the desired amount of ingredients in the aerosol forming chamber for delivery to a consumer.

Claims:

1. A cartridge comprising:
a first compartment comprising a volatile delivery enhancing compound source;
5 a second compartment comprising a medicament source;
a vaporiser for heating the medicament; and
a transfer element for conveying the medicament from the second compartment to the vaporiser.
- 10 2. A cartridge according to claim 1 further comprising an aerosol forming chamber in fluid communication with the first compartment and the second compartment.
3. A cartridge according to claim 2 further comprising at least one air inlet upstream of the first compartment and at least one air outlet downstream of the aerosol forming chamber, the at
15 least one air inlet and the at least one air outlet being arranged to define an air flow pathway extending from the at least one air inlet to the at least one air outlet via the first compartment, the vaporiser and the aerosol forming chamber.
4. A cartridge according to claim 1, 2 or 3, wherein the transfer element comprises a
20 capillary material for conveying the medicament from the second compartment to the vaporiser by capillary action.
5. A cartridge according to claim 4, wherein the capillary material is a capillary wick having a first portion extending into the second compartment and a second portion adjacent to the
25 vaporiser.
6. A cartridge according to any one of the preceding claims, wherein the second compartment comprises a sorption element with the medicament sorbed thereon.
- 30 7. A cartridge according to any one of the preceding claims, wherein the medicament comprises pure nicotine, a nicotine solution or a liquid tobacco extract.
8. A cartridge according to any one of the preceding claims, wherein the first compartment comprises a sorption element with the volatile delivery enhancing compound sorbed thereon.
- 35 9. A cartridge according to any of the preceding claims, wherein the volatile delivery enhancing compound comprises an acid selected from the group consisting of 3-methyl-2-

oxovaleric acid, pyruvic acid, 2-oxovaleric acid, 4-methyl-2-oxovaleric acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof.

10. A cartridge according to any one of the preceding claims, wherein the vaporiser
5 comprises an electrically operated heater, the heater being connectable to an electric power supply.

11. A device configured to receive a cartridge according to any of the preceding claims, the device comprising:

10 an outer housing;
a power source;
temperature controlling means for controlling the temperature of the first compartment of the cartridge;

temperature controlling means for controlling the temperature of the vaporiser for
15 heating a medicament; and

electronic circuitry configured to control power to the temperature controlling means from the power source,

wherein the electronic circuitry is configured to maintain the first compartment of the cartridge at a temperature of between about 30°C and about 50°C.

20 12. A device according to Claim 11, wherein the electronic circuitry is configured to maintain the temperature of the medicament at a temperature of between about 70°C and about 100°C.

13. An aerosol delivery system comprising:

25 a device in cooperation with a cartridge, the device or cartridge comprising a first compartment comprising a volatile delivery enhancing compound source;

the device or cartridge comprising a second compartment comprising a medicament source;

the device or cartridge comprising a vaporiser for heating the medicament; and

30 the device or cartridge further comprising a transfer element for conveying the medicament from the second compartment to the vaporiser;

wherein the device or cartridge further comprises an aerosol forming chamber in fluid communication with the first compartment and the second compartment.

35 14. An aerosol delivery system according to claim 12, wherein the device or the cartridge further comprises a mouthpiece in fluid communication with the aerosol forming chamber.

15. A method of delivering aerosolised medicament-containing particles to a user, the method comprising:

controlling the temperature of a delivery enhancing compound to between about 30°C and about 50°C to form a delivery enhancing compound-containing vapour;

5 heating a medicament to a temperature of between about 70°C and about 100°C to form a medicament-containing vapour; and

contacting the delivery enhancing compound-containing vapour with the medicament-containing vapour to form aerosolised medicament-containing particles.

- 1/2 -

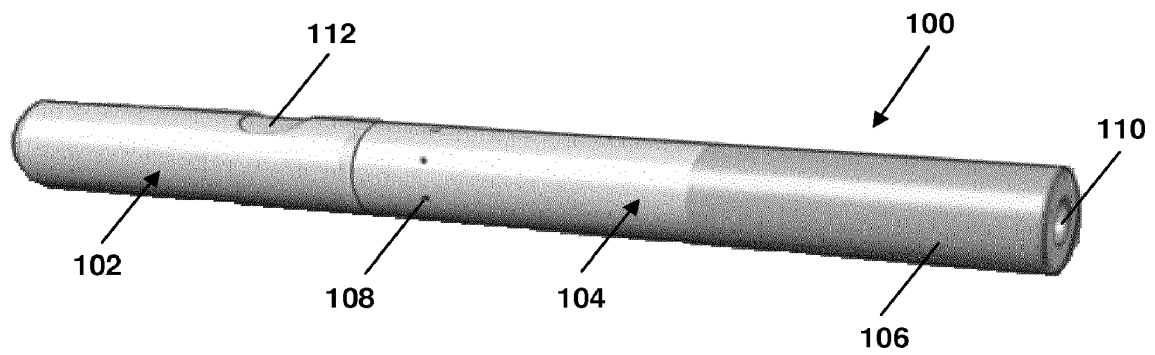


Figure 1(a)

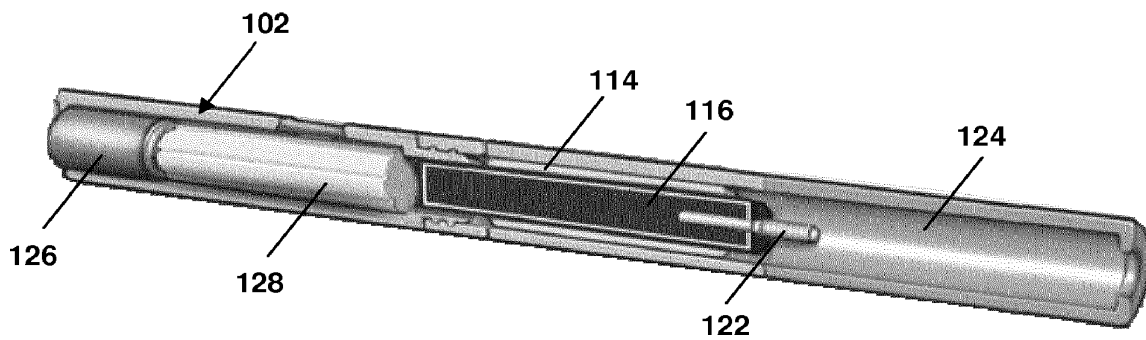


Figure 1(b)

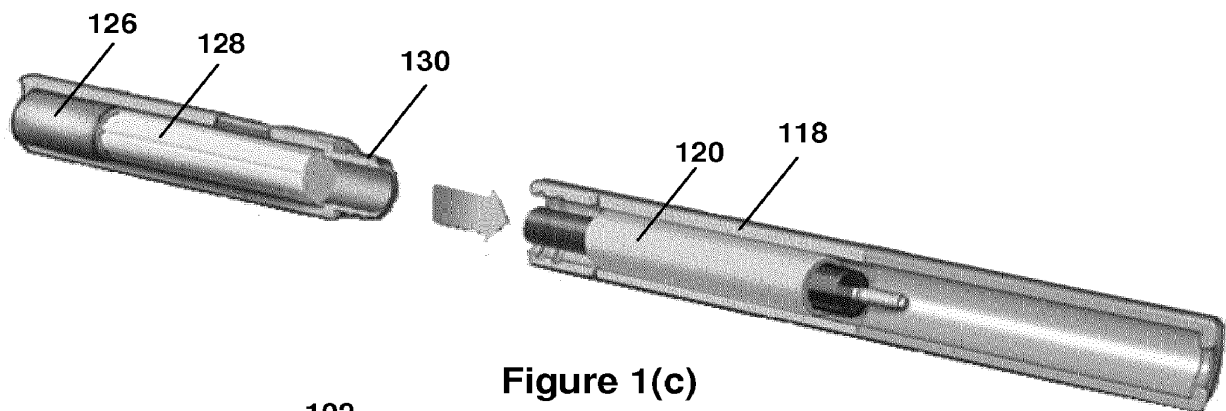


Figure 1(c)

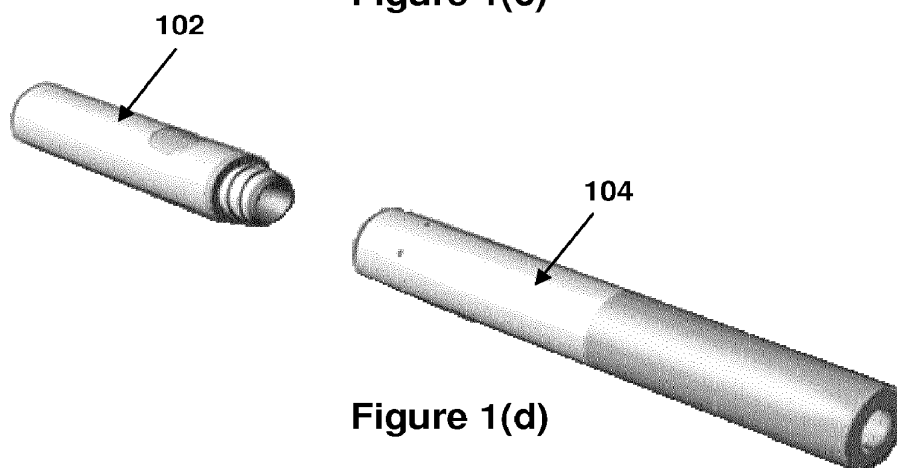
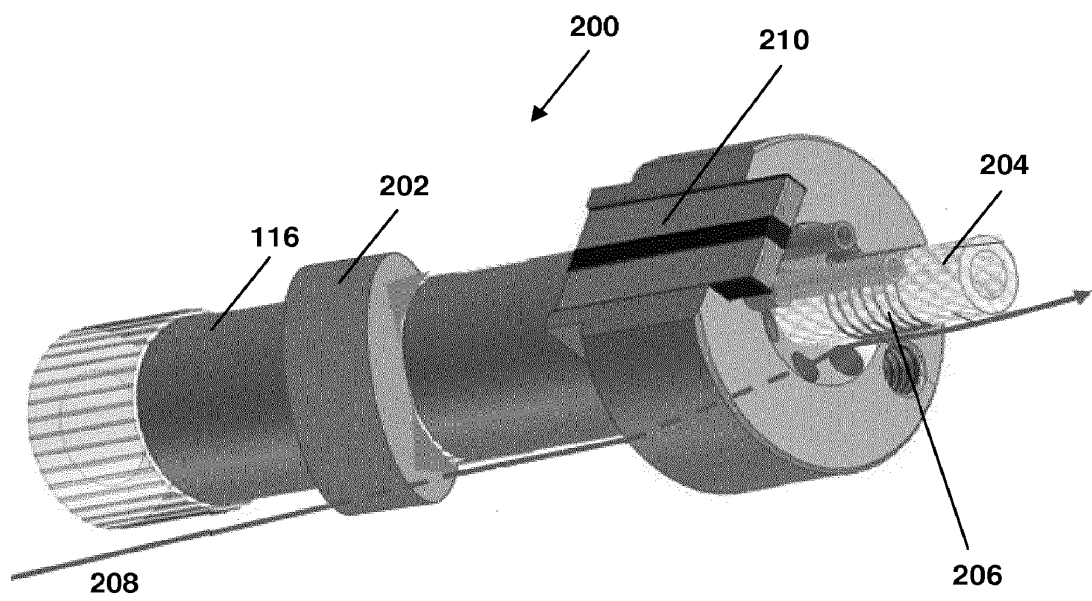


Figure 1(d)

**Figure 2**

(10) International Publication Number
WO 2014/187770 A3(43) International Publication Date
27 November 2014 (27.11.2014)

- (51) **International Patent Classification:**
A24F 47/00 (2006.01) A61M 15/00 (2006.01)
- (21) **International Application Number:**
PCT/EP2014/060225
- (22) **International Filing Date:**
19 May 2014 (19.05.2014)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
13168609.9 21 May 2013 (21.05.2013) EP
- (71) **Applicant:** PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).
- (72) **Inventors:** THORENS, Michel; Les Combremonts 24,
CH-1510 Moudon (CH). COCHAND, Olivier; Le Fau-
bourg 30, CH-2056 Dombresson (CH).
- (74) **Agent:** MILLBURN, Julie; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).
- (81) **Designated States** (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,

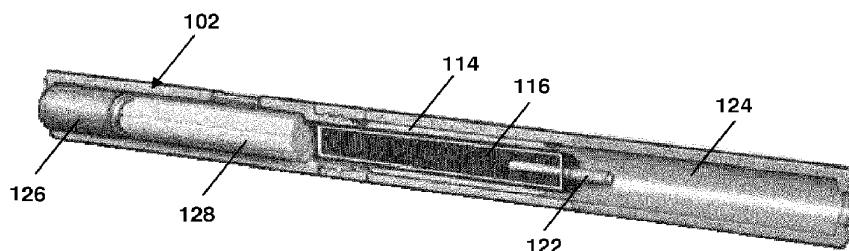
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

- (84) **Designated States** (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

- (88) **Date of publication of the international search report:**
19 March 2015

(54) **Title:** ELECTRICALLY HEATED AEROSOL DELIVERY SYSTEM**Figure 1(b)**

(57) **Abstract:** The invention relates to an aerosol delivery system for delivering aerosolised medicament particles to a user comprising a cartridge and a device configured to receive the cartridge. The cartridge comprises: a first compartment comprising a delivery enhancing compound source; a second compartment comprising a medicament source; a vaporiser for heating the medicament; and a transfer element for conveying the medicament from the second compartment to the vaporiser. The cartridge may further comprise an aerosol forming chamber in fluid communication with the first compartment and the second compartment. The device comprises: an outer housing; a power source; temperature controlling means for controlling the temperature of the first compartment of the cartridge; and electronic circuitry configured to control power to the temperature controlling means from the power source. The electronic circuitry is configured to maintain the first compartment of the cartridge at a temperature of between about 30°C and about 50°C. In use, the medicament reacts with the delivery enhancing compound in the gas phase to form aerosolised medicament-containing particles.

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/060225

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24F47/00 A61M15/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F A61M A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/107613 A1 (UNIV DUKE [US]; ROSE SETH D [US]; TURNER JAMES EDWARD [US]; MURUGESAN) 23 September 2010 (2010-09-23) paragraphs [0001], [0034], [0061], [0065] - [0067], [0071], [0198], [0199]; figures 1,2 -----	1-12, 15
X	WO 2013/030202 A1 (KRAPP RAINER [DE]; FACKLER HELMUT [DE]; RICHTER ELMAR [DE]) 7 March 2013 (2013-03-07)	1-9
A	page 1, lines 4-19 page 5, line 29 - page 7, line 13 page 21, lines 13-19 page 28, lines 7-23 claim 1; figure 1 -----	10-12



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

26 August 2014

Date of mailing of the international search report

05/02/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Kock, Søren

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/060225

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12, 15

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12, 15

Claims 1-10 pertain to a cartridge comprising two compartments, the first compartment comprising a volatile delivery enhancing compound source and the second compartment comprising a medicament source. An element for transferring the medicament from the second compartment to a vaporiser is present. Claims 11-12 pertain to a device for receiving a cartridge as set out above. The device comprises two temperature controlling means for controlling the temperature of the first compartment (comprising the volatile delivery enhancing compound source) and the second compartment (comprising the medicament source). The method of claim 15 pertains to a method of delivering aerosolised medicament-containing particles by heating a first and a second compound to different temperatures and then combining these compounds to form resulting aerosolised medicament-containing particles.

2. claims: 13, 14

A device in cooperation with an unspecified cartridge. The device comprises a first compartment and a second compartment. The first compartment of the device comprising a volatile delivery enhancing compound source and the second compartment of the device comprising a medicament source. An element for transferring the medicament from the second compartment to a vaporiser of the device is present.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/060225

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010107613 A1	23-09-2010	AU 2010226152 A1	06-10-2011
		CA 2755580 A1	23-09-2010
		CN 102355914 A	15-02-2012
		CO 6410316 A2	30-03-2012
		EP 2408494 A1	25-01-2012
		JP 2012520736 A	10-09-2012
		KR 20110139238 A	28-12-2011
		NZ 594585 A	31-01-2014
		RU 2011141824 A	27-04-2013
		SG 174867 A1	28-11-2011
		US 2012006342 A1	12-01-2012
		WO 2010107613 A1	23-09-2010

WO 2013030202 A1	07-03-2013	DE 102011111999 A1	28-02-2013
		WO 2013030202 A1	07-03-2013



(51) International Patent Classification:

A61K 9/00 (2006.01) F24J 1/00 (2006.01)
A61M 15/06 (2006.01)

(21) International Application Number:

PCT/US2014/046288

(22) International Filing Date:

11 July 2014 (11.07.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/845,333 11 July 2013 (11.07.2013) US
62/020,766 3 July 2014 (03.07.2014) US

(71) Applicant: **ALEXZA PHARMACEUTICALS, INC.**
[US/US]; 2091 Stierlin Ct., Mountain View, California
94043 (US).

(72) Inventors: **MYERS, Daniel J.**; 75 Eldora Drive, Moun-
tain View, California 94041 (US). **CASELLA, James**;
2091 Stierlin Ct., Mountain View, California 94043 (US).

(74) Agents: **SWANSON & BRATSCHUN, L.L.C.** et al.;
8210 SouthPark Terrace, Littleton, Colorado 80120 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

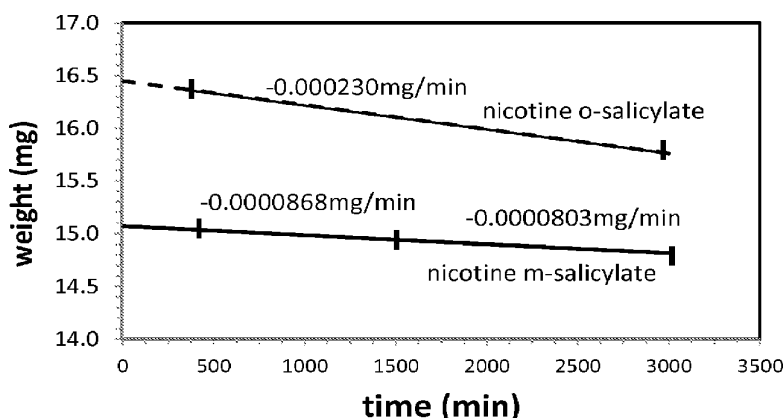
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: NICOTINE SALT WITH META-SALICYLIC ACID

Figure 6



(57) Abstract: The present disclosure relates generally to the field of nicotine delivery. The disclosure teaches a nicotine meta-salicylate. More specifically, the disclosure teaches a condensation nicotine aerosol where nicotine meta-salicylate is vaporized. This disclosure relates to aerosol nicotine delivery devices. The delivery devices can be activated by actuation mechanisms to vaporize thin films comprising a nicotine meta-salicylate. More particularly, this disclosure relates to thin films of nicotine salt with meta salicylic acid for the treatment of nicotine craving and for effecting smoking cessation.

NICOTINE SALT WITH META-SALICYLIC ACID

RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional application Ser. No. 61/845,333 entitled "Nicotine Salt with Meta-Salicylic Acid," filed July 11, 2013, Myers. This application claims priority to U.S. provisional application Ser. No. 62/020,766 entitled "Drug Delivery and Cessation System, Apparatus, and Method," filed July 3, 2014, Cassella. The entire disclosures of which are hereby incorporated by reference. Any disclaimer that may have occurred during the prosecution of the above-referenced applications is hereby expressly rescinded, and reconsideration of all relevant art is respectfully requested.

TECHNICAL FIELD

[0002] The present disclosure relates generally to the field of nicotine delivery. The disclosure teaches a nicotine meta-salicylate. More specifically, the disclosure teaches a condensation nicotine aerosol where nicotine meta-salicylate is vaporized. This disclosure relates to aerosol nicotine delivery devices. The delivery devices can be activated by actuation mechanisms to vaporize thin films comprising a nicotine meta-salicylate. More particularly, this disclosure relates to thin films of nicotine meta-salicylate for the treatment of nicotine craving and for effecting smoking cessation. The disclosure also relates to methods, systems, apparatuses, and computer software for delivering dosages of a drug to a user, and for drug cessation control, and, more particularly to methods, systems, apparatuses, and computer software for delivering dosages of nicotine to a user, and for nicotine cessation control.

BACKGROUND

[0003] Cigarette smoking provides an initial sharp rise in nicotine blood level as nicotine is absorbed through the lungs of a smoker. In general, a blood level peak produced by cigarettes of between 30-40 ng/mL is attained within 10 minutes of smoking. (Hukkanen et al., Am Soc. Pharm Exp Therap 2013) The rapid rise in nicotine blood level is postulated to be responsible for the postsynaptic effects at nicotinic cholinergic receptors in the central nervous system and at autonomic ganglia which induces the symptoms experienced by

cigarette smokers, and may also be responsible for the craving symptoms associated with cessation of smoking.

[0004] While many nicotine replacement therapies have been developed, none of the therapies appear to reproduce the pharmacokinetic profile of the systemic nicotine blood concentration provided by cigarettes. As a consequence, conventional nicotine replacement therapies have not proven to be particularly effective in enabling persons to quit smoking. For example, many commercially available products for nicotine replacement in smoking cessation therapy are intended to provide a stable baseline concentration of nicotine in the blood. Nicotine chewing gum and transdermal nicotine patches are two examples of smoking cessation products which, while providing blood concentrations of nicotine similar to that provided by cigarettes at times greater than about 30 minutes, do not reproduce the sharp initial rise in blood nicotine concentrations obtained by smoking cigarettes. Nicotine gum is an ion-exchange resin that releases nicotine slowly when a patient chews, and the nicotine present in the mouth is delivered to the systemic circulation by buccal absorption. Nicotine patches provide a consistent, steady release rate, which leads to low, stable blood levels of nicotine. Thus, both nicotine gum and transdermal nicotine do not reproduce the pharmacokinetic profile of nicotine blood levels obtained through cigarette smoking, and thus do not satisfy the craving symptoms experienced by many smokers when attempting to quit smoking.

[0005] Inhalation products which generate nicotine vapor are also ineffective as inhaled vapors are predominately absorbed through the tongue, mouth and throat, and are not deposited into the lungs. Smokeless nicotine products such as chewing tobacco, oral snuff or tobacco sachets deliver nicotine to the buccal mucosa where, as with nicotine gum, the released nicotine is absorbed only slowly and inefficiently. Nicotine blood levels from these products require approximately 30 minutes of use to attain a maximum nicotine blood concentration of approximately 12 ng/mL, which is less than half the peak value obtained from smoking one cigarette. Low nicotine blood levels obtained using a buccal absorption route may be due to first pass liver metabolism. Orally administered formulations and lozenges are also relatively ineffective.

[0006] Rapid vaporization of thin films of drugs at temperatures up to 600 °C in less than 500 msec in an air flow can produce drug aerosols having high yield and high purity with minimal degradation of the drug. Condensation drug aerosols can be used for effective pulmonary delivery of drugs using inhalation medical devices. Devices and methods in

which thin films of drugs deposited on metal substrates are vaporized by electrically resistive heating have been demonstrated. Chemically-based heat packages which can include a fuel capable of undergoing an exothermic metal oxidation-reduction reaction within an enclosure can also be used to produce a rapid thermal impulse capable of vaporizing thin films to produce high purity aerosols, as disclosed, for example in U.S. Application No. 10/850,895 entitled “Self-Contained heating Unit and Drug-Supply Unit Employing Same” filed May 20, 2004, and U.S Application No. 10/851,883, entitled “Percussively Ignited or Electrically Ignited Self-Contained Heating Unit and Drug Supply Unit Employing Same,” filed May 20, 2004, the entirety of both of which are herein incorporated by reference. These devices and methods are appropriate for use with compounds that can be deposited as physically and chemically stable solids. Unless vaporized shortly after being deposited on the metal surface, liquids can evaporate or migrate from the surface. Therefore, while such devices can be used to vaporize liquids, the use of liquid drugs can impose certain undesirable complexity. Nicotine is a liquid at room temperature with a relatively high vapor pressure. Therefore, known devices and methods are not particularly suited for producing nicotine aerosols using the liquid drug.

[0007] It is postulated that treatment of nicotine craving and smoking cessation can be addressed by treatment regimens and/or therapies that reproduce the rapid onset of high nicotine blood concentrations achieved during cigarette smoking. A cigarette smoker typically inhales about 10 times over a period of about 5 minutes. Therefore, a nicotine delivery device capable of simulating the use profile of cigarette smoking can include from 5 to 20 doses of up to about 200 μg each of nicotine, which could then be intermittently released upon request by the user.

[0008] Thus, there remains a need for a nicotine replacement therapy that provides a pharmacokinetic profile similar to that obtained by cigarette smoking, and thereby directly addresses the craving symptoms associated with the cessation of smoking.

Summary of the Embodiments

[0009] Accordingly, one aspect of the present disclosure teaches nicotine meta-salicylate. One aspect of the present disclosure provides a compound comprising a volatile nicotine meta-salicylate compound, wherein the compound is selectively vaporizable when heated.

[0010] One aspect of the present disclosure provides a nicotine delivery device comprising an electric multidose platform (EMD) as shown in figure 13.

[0011] One aspect of the present disclosure provides a nicotine delivery device comprising a housing defining an airway, wherein the airway comprises at least one air inlet and a mouthpiece having at least one air outlet, at least one heat package disposed within the airway, at least nicotine meta-salicylate disposed on the at least one heat package, and a mechanism configured to actuate the at least one heat package.

[0012] One aspect of the present disclosure provides a nicotine delivery device comprising a housing defining an airway, wherein the airway comprises at least one air inlet and a mouthpiece having at least one air outlet, at least one percussively activated heat package disposed within the airway, at least nicotine meta-salicylate disposed on the at least one percussively activated heat package, and a mechanism configured to impact the at least one percussively activated heat package. For purpose of clarity, “percussively activated heat package” herein means a heat package that has been configured so that it can be fired or activated by percussion. An “unactivated heat package” or “non-activated heat package” refers herein to a percussively activated heat package in a device, but one that is not yet positioned in the device so that it can be directly impacted and fired, although the heat package itself is configured to be activated by percussion when so positioned.

[0013] One aspect of the present disclosure provides a method of producing an aerosol of nicotine by selectively vaporizing the compound from a thin film comprising nicotine meta-salicylate.

[0014] One aspect of the present disclosure provides a method of delivering nicotine to a person comprising providing a nicotine delivery device comprising, a housing defining an airway, wherein the airway comprises at least one air inlet and a mouthpiece having at least one air outlet, at least two or more heat packages disposed within the airway, at least nicotine meta-salicylate disposed on the heat packages, and a mechanism configured to activate heat packages, inhaling through the mouthpiece, and activating the heat package, wherein the activated heat package vaporizes the at least nicotine meta-salicylate to form an aerosol comprising the nicotine in the airway which is inhaled by the person.

[0015] One aspect of the present disclosure provides a method for treating nicotine craving and smoking cessation using a nicotine aerosol.

[0016] One aspect of the present disclosure provides for tapering of the nicotine dose through behavior modification therapy, utilizing electronic dose controlling and/or tapering through dose reduction.

[0017] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of certain embodiments, as claimed.

[0018] The present invention relates to methods of manufacture and compositions which facilitate the inhalation delivery of nicotine to a patient for use as either a smoking substitute, an aid to smoking cessation, or, as will be discussed later, in the treatment of illnesses. One embodiment of the present disclosure is capable of delivering nicotine into a patient's blood in a manner which results in attainment of blood nicotine concentrations similar to the blood nicotine concentrations attained through smoking cigarettes to thereby address the physical cravings for nicotine which a smoker develops. In addition, the nicotine-containing dosage form disclosed provides a patient the opportunity, if desired, for physical manipulation and oral stimulation associated with repeated insertion and removal of the dosage form into and out of the patient's mouth to thereby address some of the psychological cravings which a smoker develops.

[0019] It is one object of the present disclosure to provide a nicotine-containing dosage form which can be utilized as part of a long-term smoking cessation program. Another object is to provide a nicotine-containing dosage form which is suitable for use as a smoking substitute whenever smoking is not allowed or desired. A further object of the disclosure is to provide a nicotine aerosol highly free of the toxins present in cigarettes. A further object of the disclosure is to provide a nicotine-containing dosage form which can maintain nicotine plasma concentrations within a range which alleviates smoking withdrawal symptoms. Another object of the present disclosure is to provide a nicotine-containing dosage form which can provide nicotine plasma concentrations similar to those achieved by smoking a cigarette, including a similar pharmacological profile of nicotine delivery. Additionally, the disclosure teaches a nicotine-containing dosage form which addresses some of the psychological needs of an individual who desires to quit smoking. The disclosure also teaches a nicotine-containing dosage form which is easy to use in order to promote patient compliance. The disclosure further teaches the cessation/diminution of the craving for a

cigarette by allowing the patient to self-titrate the amount of nicotine to overcome the person's individual craving.

[0020] The disclosure teaches a new nicotine salt, nicotine m-salicylate (nicotine meta-salicylate). It is noted that m-salicylic acid is also referred to as 3-hydroxybenzoic acid. In one aspect, the disclosure teaches a novel composition for delivery of nicotine comprising a condensation aerosol formed by volatilizing a heat stable nicotine meta-salicylate composition under conditions effective to produce a heated vapor of said nicotine meta-salicylate composition and condensing the heated vapor of the drug composition to form condensation aerosol particles, wherein said condensation aerosol particles are characterized by less than 10% nicotine degradation products, wherein the aerosol MMAD is less than 3 microns and wherein said heat stable nicotine meta-salicylate composition comprises nicotine meta-salicylate.

[0021] In some variations, the aerosol comprises at least 50% by weight of nicotine condensation particles. In other variations the aerosol comprises at least 90% or 95% by weight of the nicotine condensation particles. Similarly, in some variations, the aerosol is substantially free of thermal degradation products, and in some variations, the condensation aerosol has a MMAD in the range of 0.1-3 μm . In certain embodiments, the particles have an MMAD of less than 5 microns, preferably less than 3 microns. Preferably, the particles have a mass median aerodynamic diameter of from 0.2 to 5 microns, or most preferably from 0.2 to 3 microns. Typically, the aerosol comprises a therapeutically effective amount of nicotine and in some variations may comprise pharmaceutically acceptable excipients. In some variations, the carrier gas is air. In some variations, other gases or a combination of various gases may be used. In some variations, the percent of nicotine free base is at least 10%. In some variations, the percent of nicotine free base in the aerosol is at least 20%. In some variations, the percent of nicotine free base in the aerosol is at least 30%. In some variations, the percent of nicotine free base in the aerosol is at least 40%. In some variations, the percent of nicotine free base in the aerosol is at least 50%. In some variations, the percent of nicotine free base in the aerosol is between 1% and 10%. In some variations, the percent of nicotine free base in the aerosol is between 10% and 20%. In some variations, the percent of nicotine free base in the aerosol is between 20% and 30%. In some variations, the percent of nicotine free base in the aerosol is between 30% and 40%. In some variations, the percent of nicotine free base in the aerosol is between 40% and 50%.

[0022] In another aspect of the invention, the invention provides compositions for inhalation delivery, comprising an aerosol of vaporized nicotine condensed into particles, characterized by less than 5% drug degradation products, and wherein said aerosol has a mass median aerodynamic diameter between 0.1-3 microns.

[0023] In some variations of the aerosol compositions, the carrier gas is a non-propellant, non-organic solvent carrier gas. In some variations of the aerosol compositions, the carrier gas is air. In some variations, the aerosol is substantially free of organic solvents and propellants.

[0024] In other embodiments, aerosols of nicotine are provided that contain less than 5% nicotine degradation products, and a mixture of a carrier gas and condensation particles, formed by condensation of a vapor of nicotine in said carrier gas; wherein the MMAD of the aerosol increases over time, within the size range of 0.1 to 3 microns as said vapor cools by contact with the carrier gas.

[0025] In some variations, the aerosol comprises at least 50% by weight of nicotine condensation particles. In other variations the aerosol comprises at least 90% or 95% by weight of the nicotine condensation particles. In some variations, the MMAD of the aerosol is less than 2 microns and increases over time. In some variations, the carrier gas is air. In some variations, other gases or a combination of various gases may be used.

[0026] The condensation aerosols of the various embodiments are typically formed by preparing a film containing a nicotine meta-salicylate composition of a desired thickness on a heat-conductive and impermeable substrate and heating said substrate to vaporize said film, and cooling said vapor thereby producing aerosol particles containing said composition. Rapid heating in combination with the gas flow helps reduce the amount of decomposition. Thus, a heat source is used that typically heats the substrate to a temperature of greater than 200°C, preferably at least 250 °C, more preferably at least 300 °C or 350 °C and produces substantially complete volatilization of the nicotine meta-salicylate composition from the substrate within a period of 2 seconds, preferably, within 1 second, and more preferably, within 0.5 seconds.

[0027] Typically, the gas flow rate over the vaporizing compound is between about 1 and 10 L/minute. Further, the gas flow rate over the vaporizing compound can be between about 2 and 8 L/minute.

[0028] The film thickness is such that an aerosol formed by vaporizing the nicotine meta-salicylate by heating the substrate and condensing the vaporized compound contains

10% by weight or less nicotine-degradation product. The use of thin films allows a more rapid rate of vaporization and hence, generally, less thermal nicotine degradation. Typically, the film has a thickness between 0.05 and 30 microns. In some variations, the film has a thickness between 0.5 and 25 microns. In some variations the film has a thickness of about 21 microns. The selected area of the substrate surface expanse is such as to yield an effective dose of the nicotine aerosol.

[0029] In a related aspect, the disclosure teaches kits for delivering a nicotine condensation aerosol that typically comprises a composition devoid of solvents and excipients and comprising a heat stable nicotine meta-salicylate, and a device for forming and delivering via inhalation a condensation aerosol. The device for forming a drug aerosol typically comprises an element configured to heat the composition to form a vapor, an element allowing the vapor to condense to form a condensation aerosol, and an element permitting a user to inhale the condensation aerosol. Typically, the element configured to heat the composition comprises a heat-conductive substrate and formed on the substrate is typically a nicotine meta-salicylate composition film containing an effective dose of nicotine when the nicotine is administered in an aerosol form. A heat source in the device is operable to supply heat to the substrate to produce a substrate temperature, typically that is greater than 300°C, to substantially volatilize the nicotine meta-salicylate composition film from the substrate in a period of 2 seconds or less, more preferably, in a period of 500 milliseconds or less. The device may further comprise features such as breath-actuation, lockout elements, dose counting/logging or tapering methods.

[0030] In yet another aspect, the disclosure teaches kits for delivering nicotine aerosol comprising a thin film of a nicotine meta-salicylate composition and a device for dispensing said film as a condensation aerosol. Typically, the film thickness is between 0.5 and 30 microns. The film can comprise pharmaceutically acceptable excipients and is typically heated at a rate so as to substantially volatilize the film in 500 milliseconds or less.

[0027] To achieve the foregoing objects, and in accordance with the invention as embodied and broadly described herein, a nicotine-containing dosage form is provided. The dosage form is configured having a nicotine-containing composition wherein the nicotine composition comprises nicotine meta-salicylate.

[0028] These and other objects and features of the invention will be more fully appreciated when the following detailed description of the invention is read in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0031] Fig. 1 is ortho-salicylic acid, para-salicylic acid and 3-hydroxybenzoic acid (meta-salicylic acid).
- [0032] Fig. 2 shows a typical calorimetric scan of nicotine m-salicylate powder.
- [0033] Fig. 3 shows the ortho isomer.
- [0034] Fig. 4 shows the para isomer.
- [0035] Fig. 5 shows the meta isomer.
- [0036] Fig. 6 is a thermogravimetric analysis plot showing the isothermal mass loss of the nicotine meta-salicylate is less than that of nicotine ortho-salicylate.
- [0037] Fig. 7 shows thermogravimetric analysis. Scanning data from room temperature to 500°C, showing minimal charring of the acid after exposure to high temperatures.
- [0038] Fig. 8 shows a chromatogram of a typical sample run on the nicotine impurity method.
- [0039] Fig. 9 shows a chromatogram of a typical sample run on the m-salicylate impurity method.
- [0040] Fig. 10 shows the particle size distribution amongst the various impactor stages.
- [0041] Fig. 11 shows particle size distributions.
- [0042] Fig. 12 shows nicotine mass loss over time.
- [0043] Fig. 13 shows m-salicylic acid mass loss over time.
- [0044] Fig. 14 shows unpouched stability summary.
- [0045] Fig. 15 shows unpouched stability summary.
- [0046] Fig. 16 Nicotine device 1.
- [0047] Fig. 17 Nicotine device 2.
- [0048] Figure 18 Nicotine device 3.
- [0049] Figure 19 Nicotine device 4.
- [0050] Reference will now be made in detail to embodiments of the present disclosure. While certain embodiments of the present disclosure will be described, it will be understood that it is not intended to limit the embodiments of the present disclosure to those described embodiments. To the contrary, reference to embodiments of the present disclosure

is intended to cover alternatives, modifications, and equivalents as may be included within the spirit and scope of the embodiments of the present disclosure as defined by the appended claims.

DESCRIPTION OF VARIOUS EMBODIMENTS

Definitions

[0051] As defined herein, the following terms shall have the following meanings when reference is made to them throughout the specification.

[0052] “Aerodynamic diameter” of a given particle refers to the diameter of a spherical droplet with a density of 1 g/mL (the density of water) that has the same settling velocity as the given particle.

[0053] “Aerosol” refers to a collection of solid or liquid particles suspended in a gas.

[0054] “Aerosol mass concentration” refers to the mass of particulate matter per unit volume of aerosol.

[0055] “Condensation aerosol” refers to an aerosol that has been formed by the vaporization of a composition and subsequent cooling of the vapor, such that the vapor condenses to form particles.

[0056] “Decomposition index” refers to a number derived from an assay. The number is determined by subtracting the purity of the generated aerosol, expressed as a fraction, from 1.

[0057] “Drug” means any substance that is used in the prevention, diagnosis, alleviation, treatment or cure of a condition. The drug is preferably in a form suitable for thermal vapor delivery, such as an ester, free acid, or free base form. The terms “drug”, “compound”, and “medication” are used herein interchangeably. As described in throughout the specification, the term drug includes nicotine and nicotine meta-salicylate.

[0058] “Drug composition” refers to a composition that comprises only pure drug, two or more drugs in combination, or one or more drugs in combination with additional components. Additional components can include, for example, pharmaceutically acceptable excipients, carriers, and surfactants.

[0059] “Drug degradation product” or “thermal degradation product” are used interchangeably and means any byproduct, which results from heating the drug(s) and is not responsible for producing a therapeutic effect.

[0060] “Drug supply article” or “drug supply unit” are used interchangeably and refers to a substrate with at least a portion of its surface coated with one or more drug compositions. Drug supply articles of the invention may also include additional elements such as, for example, but not limitation, a heating element.

[0061] “Effective amount of nicotine” means the amount of nicotine required to achieve the effect achieved from nicotine through smoking cigarettes. The effect could be any effect ranging from symptom amelioration with regard to withdraw to symptom treatment. In one embodiment, the effective amount of nicotine is between 50 to 200 $\mu\text{g}/\text{dose}$.

[0062] “Fraction drug degradation product” refers to the quantity of drug degradation products present in the aerosol particles divided by the quantity of drug plus drug degradation product present in the aerosol, *i.e.* (sum of quantities of all drug degradation products present in the aerosol)/((quantity of drug(s) present in the aerosol) + (sum of quantities of all drug degradation products present in the aerosol)). The term “percent drug degradation product” as used herein refers to the fraction drug degradation product multiplied by 100%, whereas “purity” of the aerosol refers to 100% minus the percent drug degradation products.

[0063] “Heat stable drug” refers to a drug that has a $\text{TSR} \geq 9$ when vaporized from a film of some thickness between 0.05 μm and 20 μm .

[0064] “Mass median aerodynamic diameter” or “MMAD” of an aerosol refers to the aerodynamic diameter for which half the particulate mass of the aerosol is contributed by particles with an aerodynamic diameter larger than the MMAD and half by particles with an aerodynamic diameter smaller than the MMAD.

[0065] “Number concentration” refers to the number of particles per unit volume of aerosol.

[0066] “Purity” as used herein, with respect to the aerosol purity, means the fraction of drug composition in the aerosol/ the fraction of drug composition in the aerosol plus drug degradation products. Thus purity is relative with regard to the purity of the starting material. For example, when the starting drug or drug composition used for substrate coating contained detectable impurities, the reported purity of the aerosol does not include those impurities present in the starting material that were also found in the aerosol, *e.g.*, in certain cases if the starting material contained a 1% impurity and the aerosol was found to contain the identical 1% impurity, the aerosol purity may nevertheless be reported as >99 % pure, reflecting the

fact that the detectable 1% purity was not produced during the vaporization-condensation aerosol generation process.

[0067] “Settling velocity” refers to the terminal velocity of an aerosol particle undergoing gravitational settling in air.

[0068] “Support” refers to a material on which the composition is adhered, typically as a coating or thin film. The term “support” and “substrate” are used herein interchangeably.

[0069] “Substantially free of” means that the material, compound, aerosol, etc., being described is at least 95% free of the other component from which it is substantially free.

[0070] “Typical patient tidal volume” refers to 1 L for an adult patient and 15 mL/kg for a pediatric patient.

[0071] “Therapeutically effective amount” means the amount required to achieve a therapeutic effect. The therapeutic effect could be any therapeutic effect ranging from prevention, symptom amelioration, symptom treatment, to disease termination or cure.

[0072] “Thermal stability ratio” or “TSR” means the $\% \text{ purity} / (100\% - \% \text{ purity})$ if the $\% \text{ purity}$ is $< 99.9\%$, and 1000 if the $\% \text{ purity}$ is $\geq 99.9\%$. For example, a respiratory drug vaporizing at 90% purity would have a TSR of 9.

[0073] “4 μm thermal stability ratio” or “4TSR” means the TSR of a drug determined by heating a drug-comprising film of about 4 microns in thickness under conditions sufficient to vaporize at least 50% of the drug in the film, collecting the resulting aerosol, determining the purity of the aerosol, and using the purity to compute the TSR. In such vaporization, generally the about 4-micron thick drug film is heated to around 350°C but not less than 200°C for around 1 second to vaporize at least 50% of the drug in the film.

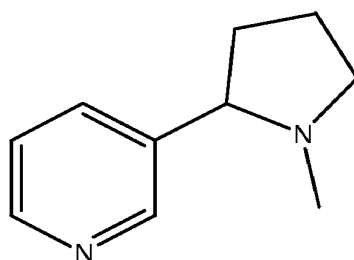
[0074] “1.5 μm thermal stability ratio” or “1.5TSR” means the TSR of a drug determined by heating a drug-comprising film of about 1.5 microns in thickness under conditions sufficient to vaporize at least 50% of the drug in the film, collecting the resulting aerosol, determining the purity of the aerosol, and using the purity to compute the TSR. In such vaporization, generally the about 1.5-micron thick drug film is heated to around 350°C but not less than 200°C for around 1 second to vaporize at least 50% of the drug in the film.

[0075] “0.5 μm thermal stability ratio” or “0.5TSR” means the TSR of a drug determined by heating a drug-comprising film of about 0.5 microns in thickness under conditions sufficient to vaporize at least 50% of the drug in the film, collecting the resulting aerosol, determining the purity of the aerosol, and using the purity to compute the TSR. In

such vaporization, generally the about 0.5-micron thick drug film is heated to around 350°C but not less than 200°C for around 1 second to vaporize at least 50% of the drug in the film.

[0076] “Vapor” refers to a gas, and “vapor phase” refers to a gas phase. The term “thermal vapor” refers to a vapor phase, aerosol, or mixture of aerosol-vapor phases, formed preferably by heating.

[0077] Nicotine is a heterocyclic compound that can exist in both a free base and salt forms. The free base form has the following structure:



[0078] At 25 °C, nicotine is a colorless to pale yellow volatile liquid. Nicotine has a melting point of -79 °C, a boiling point at 247 °C, and a vapor pressure of 0.0425 mmHg at 25 °C. The liquid nature prevents formation of stable films and the high vapor pressure can result in evaporation during shelf-life storage. While various approaches for preventing nicotine evaporation and degradation during shelf-life storage have been considered, for example, delivery from a reservoir via ink jet devices, chemical encapsulation of nicotine as a cyclodextrin complex, and nicotine containment in blister packs, such implementations have not been demonstrated to be amendable to low-cost manufacturing, nor easy to reduce to practice in actual devices.

Nicotine Meta-Salicylate

[0079] The structure of meta-salicylic acid, also known as 3-hydroxybenzoic acid, is shown in Figure 2. This disclosure teaches a nicotine salt with the meta-salicylic acid. The synthesis of nicotine meta-salicylate is described in Example 1.

[0080] The nicotine meta-salicylate has two potentially important advantages over the commercially available nicotine ortho-salicylate. First, thermogravimetric analysis data show that isothermal mass loss of the nicotine meta-salicylate can be less than that of the nicotine ortho-salicylate. For example, at storage temperatures between 40-60°C, nicotine mass loss from nicotine meta-salicylate was about 2-3X less than nicotine ortho-salicylate.

[0081] Mass loss due to evaporation of the nicotine and/or salicylic acid is detrimental in view of the product's stability, i.e., the ability to provide consistent dosing of the drug over the shelf life of the product. The meta-salicylate salt is less prone to thermal degradation during vaporization, particularly with regards to formation of phenol. This is another distinct advantage of the present disclosure. The position of the hydroxyl group on the salicylic acid can affect the likelihood of the decarboxylation of salicylic acid into phenol by contributing (or not contributing) to resonance stabilization of an ion or free radical. The ortho (and para) isomers have resonance structures where the negative charge is localized on the oxygen atom, whereas this structure cannot form for the meta isomer. This structure increases the stability of the ion/radical and therefore increases the likelihood or rate of the phenol formation from ortho- or para-salicylic acid.

Aerosol Composition

[0082] The compositions described herein typically comprise nicotine compounds. The compositions may comprise other compounds as well. For example, the composition may comprise a mixture of drug compounds, a mixture of a nicotine compound and a pharmaceutically acceptable excipient, or a mixture of a nicotine compound with other compounds having useful or desirable properties. The composition may comprise a pure nicotine compound as well. In preferred embodiments, the composition consists essentially of pure nicotine meta-salicylate and contains no propellants or solvents.

[0083] Additionally, pharmaceutically acceptable carriers, surfactants, enhancers, and inorganic compounds may be included in the composition. Examples of such materials are known in the art.

[0084] In some variations, the aerosols are substantially free of organic solvents and propellants. Additionally, water is typically not added as a solvent for the nicotine meta-salicylate, although water from the atmosphere may be incorporated in the aerosol during formation, in particular, while passing air over the film and during the cooling process. In other variations, the aerosols are completely devoid of organic solvents and propellants. In yet other variations, the aerosols are completely devoid of organic solvents, propellants, and any excipients. These aerosols comprise only pure drug, less than 10% drug degradation products, and a carrier gas, which is typically air.

[0085] Typically, the drug has a decomposition index less than 0.15. Preferably, the drug has a decomposition index less than 0.10. More preferably, the drug has a decomposition index less than 0.05. Most preferably, the drug has a decomposition index less than 0.025

[0086] In some variations, the condensation aerosol comprises at least 5% by weight of condensation drug aerosol particles. In other variations, the aerosol comprises at least 10%, 20%, 30%, 40%, 50%, 60%, or 75% by weight of condensation drug aerosol particles. In still other variations, the aerosol comprises at least 95%, 99%, or 99.5% by weight of condensation aerosol particles.

[0087] In some variations, the condensation aerosol particles comprise less than 10% by weight of a thermal degradation product. In other variations, the condensation drug aerosol particles comprise less than 5%, 1%, 0.5%, 0.1%, or 0.03% by weight of a thermal degradation product.

[0088] In certain embodiments of the disclosure, the drug aerosol has a purity of between 90% and 99.8%, or between 93% and 99.7%, or between 95% and 99.5%, or between 96.5% and 99.2%. In certain embodiments of the disclosure, the drug aerosol has percent of freebase nicotine in the aerosol of between 90% and 99.8%, or between 93% and 99.7%, or between 95% and 99.5%, or between 96.5% and 99.2%.

[0089] Typically, the aerosol has a number concentration greater than 10^6 particles/mL. In other variations, the aerosol has a number concentration greater than 10^7 particles/mL. In yet other variations, the aerosol has a number concentration greater than 10^8 particles/mL, greater than 10^9 particles/mL, greater than 10^{10} particles/mL, or greater than 10^{11} particles/mL.

[0090] The gas of the aerosol typically is air. Other gases, however, can be used, in particular inert gases, such as argon, nitrogen, helium, and the like. The gas can also include vapor of the composition that has not yet condensed to form particles. Typically, the gas does not include propellants or vaporized organic solvents. In some variations, the condensation aerosol comprises at least 5% by weight of condensation drug aerosol particles. In other variations, the aerosol comprises at least 10%, 20%, 30%, 40%, 50%, 60%, or 75% by weight of condensation drug aerosol particles. In still other variations, the aerosol comprises at least 95%, 99%, or 99.5% by weight of condensation aerosol particles.

[0091] In some variations the condensation drug aerosol has a MMAD in the range of about 0.01-3 μm . In some variations the condensation drug aerosol has a MMAD in the

range of about 0.1-3 μm . In some variations the geometric standard deviation around the MMAD of the condensation drug aerosol particles is less than 3.0. In other variations, the geometric standard deviation around the MMAD of the condensation drug aerosol particles is less than 2.5, or less than 2.0.

[0092] In certain embodiments of the invention, the drug aerosol comprises one or more drugs having a 4TSR of at least 5 or 10, a 1.5TSR of at least 7 or 14, or a 0.5TSR of at least 9 or 18. In other embodiments of the invention, the drug aerosol comprises one or more drugs having a 4TSR of between 5 and 100 or between 10 and 50, a 1.5TSR of between 7 and 200 or between 14 and 100, or a 0.5TSR of between 9 and 900 or between 18 and 300.

Formation of Condensation Aerosols

[0093] Any suitable method may be used to form the condensation aerosols described herein. One such method involves the heating of a composition to form a vapor, followed by cooling of the vapor so that it forms an aerosol (*i.e.*, a condensation aerosol). Methods have been previously described in US. Patent No. 7,090,830. This reference is hereby incorporated by reference in its entirety.

[0094] Typically, the composition is coated on a substrate, and then the substrate is heated to vaporize the composition. The substrate may be of any geometry and be of a variety of different sizes. It is often desirable that the substrate provide a large surface to volume ratio (*e.g.*, greater than 100 per meter) and a large surface to mass ratio (*e.g.*, greater than 1 cm^2 per gram). The substrate can have more than one surface

[0095] A substrate of one shape can also be transformed into another shape with different properties. For example, a flat sheet of 0.25 mm thickness has a surface to volume ratio of approximately 8,000 per meter. Rolling the sheet into a hollow cylinder of 1 cm diameter produces a support that retains the high surface to mass ratio of the original sheet but has a lower surface to volume ratio (about 400 per meter).

[0096] A number of different materials may be used to construct the substrate. Typically, the substrates are heat-conductive and include metals, such as aluminum, iron, copper, stainless steel, and the like, alloys, ceramics, and filled polymers. In one variation, the substrate is stainless steel. Combinations of materials and coated variants of materials may be used as well.

[0097] When it is desirable to use aluminum as a substrate, aluminum foil is a suitable material. Examples of alumina and silicon based materials BCR171 (an alumina of

defined surface area greater than 2 m²/g from Aldrich, St. Louis, MO) and a silicon wafer as used in the semiconductor industry.

[0098] Typically it is desirable that the substrate have relatively few, or substantially no, surface irregularities. Although a variety of supports may be used, supports that have an impermeable surface, or an impermeable surface coating, are typically desirable. Illustrative examples of such supports include metal foils, smooth metal surfaces, nonporous ceramics, and the like. Alternatively, or in addition, to preferred substrates having an impermeable surface, the substrate surface expanse is characterized by a contiguous surface area of about 20 mm². Alternatively, or in addition, to preferred substrates having an impermeable surface, the substrate surface expanse is characterized by a contiguous surface area of greater than 1 mm², preferably 10 mm², more preferably 50 mm² and still more preferably 100 mm², and a material density of greater than 0.5 g/cc. In contrast, non-preferred substrates typically have a substrate density of less than 0.5 g/cc, such as, for example, yarn, felts and foam, or have a surface area of less than 1 mm²/particle such as, for example small alumina particles, and other inorganic particles, as it is difficult on these types of surfaces to generate therapeutic quantities of a drug aerosol with less than 10% drug degradation via vaporization.

[0099] In one variation, the disclosure teaches a stainless steel foil substrate. A hollow, stainless steel tube may be used as the drug-film substrate. In other variations, aluminum foil is used as a substrate for testing drug.

[00100] The composition is typically coated on the solid support in the form of a film. The film may be coated on the solid support using any suitable method. The method suitable for coating is often dependent upon the physical properties of the compound and the desired film thickness. One exemplary method of coating a composition on a solid support is by preparing a solution of compound (alone or in combination with other desirable compounds) in a suitable solvent, applying the solution to the exterior surface of the solid support, and then removing the solvent (*e.g.*, via evaporation, etc.) thereby leaving a film on the support surface.

[00101] Common solvents include methanol, dichloromethane, methyl ethyl ketone, diethyl ether, acetone, ethanol, isopropyl alcohol, 3:1 chloroform:methanol mixture, 1:1 dichloromethane: methyl ethyl ketone mixture, dimethylformamide, and deionized water. In some instances (*e.g.*, when triamterene is used), it is desirable to use a solvent such as formic acid. Sonication may also be used as necessary to dissolve the compound.

[00102] The composition may also be coated on the solid support by dipping the support into a composition solution, or by spraying, brushing or otherwise applying the solution to the support. Alternatively, a melt of the drug can be prepared and applied to the support. For drugs that are liquids at room temperature, thickening agents can be mixed with the drug to permit application of a solid drug film.

[00103] The film can be of varying thickness depending on the compound and the maximum amount of thermal degradation desired. In one method, the heating of the composition involves heating a thin film of the composition having a thickness between about 0.1 μ m-30 μ m to form a vapor. In yet other variations, the composition has a film thickness between about 0.5 μ m-21 μ m. Most typically, the film thickness vaporized is between 0.5 μ m-25 μ m.

[00104] The support on which the film of the composition is coated can be heated by a variety of means to vaporize the composition. Exemplary methods of heating include the passage of current through an electrical resistance element, absorption of electromagnetic radiation (*e.g.*, microwave or laser light) and exothermic chemical reactions (*e.g.*, exothermic solvation, hydration of pyrophoric materials, and oxidation of combustible materials). Heating of the substrate by conductive heating is also suitable. One exemplary heating source is described in U.S. patent application for SELF-CONTAINED HEATING UNIT AND DRUG-SUPPLY UNIT EMPLOYING SAME, USSN 60/472,697 filed May 21, 2003. The description of the exemplary heating source disclosed therein, is hereby incorporated by reference.

[00105] Heat sources typically supply heat to the substrate at a rate that achieves a substrate temperature of at least 200° C, preferably at least 250° C, or more preferably at least 300° C or 350° C, and produces substantially complete volatilization of the drug composition from the substrate within a period of 2 seconds, preferably, within 1 second, or more preferably within 0.5 seconds. Suitable heat sources include resistive heating devices which are supplied current at a rate sufficient to achieve rapid heating, *e.g.*, to a substrate temperature of at least 200° C, 250° C, 300° C, or 350° C preferably within 50-500 ms, more preferably in the range of 50-200 ms. Heat sources or devices that contain a chemically reactive material which undergoes an exothermic reaction upon actuation, *e.g.*, by a spark or heat element, such as flashbulb type heaters of the type described in several examples, and the heating source described in the above-cited U.S. patent application for SELF-CONTAINED HEATING UNIT AND DRUG-SUPPLY UNIT EMPLOYING SAME, are

also suitable. In particular, heat sources that generate heat by exothermic reaction, where the chemical "load" of the source is consumed in a period of between 50-500 msec or less are generally suitable, assuming good thermal coupling between the heat source and substrate.

[00106] When heating the thin film of the composition, to avoid decomposition, it is desirable that the vaporized compound should transition rapidly from the heated surface or surrounding heated gas to a cooler environment. This may be accomplished not only by the rapid heating of the substrate, but also by the use of a flow of gas across the surface of the substrate. While a vaporized compound from a surface may transition through Brownian motion or diffusion, the temporal duration of this transition may be impacted by the extent of the region of elevated temperature at the surface, which is established by the velocity gradient of gases over the surface and the physical shape of surface. Typical gas-flow rates used to minimize such decomposition and to generate a desired particle size are in the range of 1-10 L/minute.

[00107] The aerosol particles for administration can typically be formed using any of the describe methods at a rate of greater than 10^8 inhalable particles per second. In some variations, the aerosol particles for administration are formed at a rate of greater than 10^9 or 10^{10} inhalable particles per second. Similarly, with respect to aerosol formation (*i.e.*, the mass of aerosolized particulate matter produced by a delivery device per unit time) the aerosol may be formed at a rate greater than 0.25 mg/second, greater than 0.5 mg/second, or greater than 1 or 2 mg/second. Further, with respect to aerosol formation, focusing on the drug aerosol formation rate (*i.e.*, the rate of drug compound released in aerosol form by a delivery device per unit time), the drug may be aerosolized at a rate greater than 0.05 mg drug per second, greater than 0.1 mg drug per second, greater than 0.5 mg drug per second, or greater than 1 or 2 mg drug per second.

[00108] In some variations, the drug condensation aerosols are formed from compositions that provide at least 5% by weight of drug condensation aerosol particles. In other variations, the aerosols are formed from compositions that provide at least 10%, 20%, 30%, 40%, 50%, 60%, or 75% by weight of drug condensation aerosol particles. In still other variations, the aerosols are formed from compositions that provide at least 95%, 99%, or 99.5% by weight of drug condensation aerosol particles.

[00109] In some variations, the drug condensation aerosol particles when formed comprise less than 10% by weight of a thermal degradation product. In other variations, the

drug condensation aerosol particles when formed comprise less than 5%, 1%, 0.5%, 0.1%, or 0.03% by weight of a thermal degradation product.

[00110] In some variations the drug condensation aerosols are produced in a gas stream at a rate such that the resultant aerosols have a MMAD in the range of about 0.1-3 μm . In some variations the geometric standard deviation around the MMAD of the drug condensation aerosol particles is less than 3.0. In other variations, the geometric standard deviation around the MMAD of the drug condensation aerosol particles is less than 2.5, or less than 2.0.

Delivery Devices

[00111] The delivery devices described herein for administering a condensation drug aerosol typically comprise an element for heating the composition to form a vapor and an element allowing the vapor to cool, thereby forming a condensation aerosol. These aerosols are generally delivered via inhalation to lungs of a patient, for local or systemic treatment. Alternatively, however, the condensation aerosols of the invention can be produced in an air stream, for application of drug-aerosol particles to a target site. For example, a stream of air carrying drug-aerosol particles can be applied to treat an acute or chronic skin condition, can be applied during surgery at the incision site, or can be applied to an open wound. The delivery device may be combined with a composition comprising a drug in unit dose form for use as a kit.

[00112] The devices described herein may additionally contain a variety of components to facilitate aerosol delivery. For instance, the device may include any component known in the art to control the timing of drug aerosolization relative to inhalation (*e.g.*, breath-actuation). Similarly, the device may include a component to provide feedback to patients on the rate and/or volume of inhalation, or a component to prevent excessive use (*i.e.*, “lockout” feature). The device may further comprise features such as dose counting/logging or tapering methods. In addition, the device may further include a component to prevent use by unauthorized individuals, and a component to record dosing histories. These components may be used alone, or in combination with other components. Additionally, the devices may contain features to allow for the tapering off of nicotine dose.

[00113] The element that allows cooling may be of any configuration. For example, it may be an inert passageway linking the heating means to the inhalation means. Similarly, the element permitting inhalation by a user may be of any configuration. For example, it may be

an exit portal that forms a connection between the cooling element and the user's respiratory system.

[00114] Typically, the drug supply article is heated to a temperature sufficient to vaporize all or a portion of the film, so that the composition forms a vapor that becomes entrained in a stream of air during inhalation. As noted above, heating of the drug supply article may be accomplished using, for example, an electrically-resistive wire embedded or inserted into the substrate and connected to a battery disposed in the housing. The heating can be actuated, for example, with a button on the housing or via breath actuation, as is known in the art.

[00115] Another device that may be used to form and deliver the aerosols described herein is as follows. The device comprises an element for heating a composition to form a vapor, an element allowing the vapor to cool, thereby forming a condensation aerosol, and an element permitting a user to inhale the aerosol. The device also comprises an upper external housing member and a lower external housing member that fit together.

[00116] The downstream end of each housing member is gently tapered for insertion into a user's mouth. The upstream end of the upper and lower housing members are slotted (either one or both are slotted), to provide for air intake when a user inhales. The upper and lower housing members when fitted together define a chamber. Positioned within chamber is a drug supply unit.

[00117] The solid support may be of any desirable configuration. At least a portion of the surface of the substrate is coated with a composition film. With the case of the thermite-type heating source, the interior region of the substrate contains a substance suitable to generate heat. The substance can be a solid chemical fuel, chemical reagents that mix exothermically, electrically resistive wire, etc. A power supply source, if needed for heating, and any necessary valving for the inhalation device may be contained in end piece. A power supply source may be a piece that mates with the drug supply unit.

[00118] In one variation of the devices used, the device includes a drug composition delivery article composed of the substrate, a film of the selected drug composition on the substrate surface, and a heat source for supplying heat to the substrate at a rate effective to heat the substrate to a temperature greater than 200°C or in other embodiments to a temperature greater than 250 °C, 300 °C or 350 °C, and to produce substantially complete volatilization of the drug composition within a period of 2 seconds or less.

[00119] Other drug supply articles that may be used in combination with the devices described herein. Various methods of coatings are known in the art and/or have been described above.

[00120] The illustrative heating element shown as an electrical resistive wire that produces heat when a current flows through it, but as noted above, a number of different heating methods and corresponding devices are acceptable. For example, acceptable heat sources can supply heat to the drug supply article at rates that rapidly achieve a temperature sufficient to completely vaporize the composition from the support surface. For example, heat sources that achieve a temperature of 200° C to 500 °C or more within a period of 2 seconds are typical, although it should be appreciated that the temperature chosen will be dependent upon the vaporization properties of the composition, but is typically heated to a temperature of at least about 200°C, preferably of at least about 250 °C, more preferably at least about 300°C or 350°C. Heating the substrate produces a drug composition vapor that in the presence of the flowing gas generates aerosol particles in the desired size range. The presence of the gas flow is generally prior to, simultaneous with, or subsequent to heating the substrate. In one embodiment, the substrate is heated for a period of less than about 1 second, and more preferably for less than about 500 milliseconds, still more preferably for less than about 200 milliseconds. The drug-aerosol particles are inhaled by a subject for delivery to the lung.

[00121] The device may also include a gas-flow control valve disposed upstream of the solid support, for limiting gas-flow rate through the condensation region. The gas-flow valve may, for example, include an inlet port communicating with the chamber, and a deformable flap adapted to divert or restrict airflow away from the port increasingly, with increasing pressure drop across the valve. Similarly, the gas-flow valve may include an actuation switch. In this variation, the valve movement would be in response to an air pressure differential across the valve, which for example, could function to close the switch. The gas-flow valve may also include an orifice designed to limit airflow rate into the chamber.

[00122] The device may also include a bypass valve communicating with the chamber downstream of the unit for offsetting the decrease in airflow produced by the gas-flow control valve, as the user draws air into the chamber. In this way, the bypass valve could cooperate with the gas-control valve to control the flow through the condensation region of the chamber as well as the total amount of air being drawn through the device. Thus the total volumetric

airflow through the device in this variation would be the sum of the volumetric airflow rate through the gas-control valve and the volumetric airflow rate through the bypass valve.

[00123] The gas control valve could, for example, function to limit air drawn into the device to a preselected level, *e.g.*, 15 L/minute. In this way, airflow for producing particles of a desired size may be preselected and produced. For example, once this selected airflow level is reached, additional air drawn into the device would create a pressure drop across the bypass valve, which in turn would accommodate airflow through the bypass valve into the downstream end of the device adjacent the user's mouth. Thus, the user senses a full breath being drawn in, with the two valves distributing the total airflow between desired airflow rate and bypass airflow rate.

[00124] These valves may be used to control the gas velocity through the condensation region of the chamber and hence to control the particle size of the aerosol particles produced. Typically, the faster the airflow, the smaller the particles are. Thus, to achieve smaller or larger particles, the gas velocity through the condensation region of the chamber may be altered by modifying the gas-flow control valve to increase or decrease the volumetric airflow rate. For example, to produce condensation particles in the size range of about 1-3.5 μm MMAD, a chamber having substantially smooth-surfaced walls would have a selected gas-flow rate in the range of 1-10 L/minute.

[00125] Additionally, as will be appreciated by one of skill in the art, particle size may be altered by modifying the cross-section of the chamber condensation region to increase or decrease linear gas velocity for a given volumetric flow rate, and/or the presence or absence of structures that produce turbulence within the chamber. Thus, for example to produce condensation particles in the size range 10-100 nm MMAD, the chamber may provide gas-flow barriers for creating air turbulence within the condensation chamber. These barriers are typically placed within a few thousandths of an inch from the substrate surface. Particle size is discussed in more detail below.

Drug Composition Film Thickness

[00126] Typically, the drug composition film coated on the solid support has a thickness of between about 0.05-30 μm , and typically a thickness between 0.1-30 μm . More typically, the thickness is between about 0.2-30 μm ; even more typically, the thickness is between about 0.5-30 μm , and most typically, the thickness is between about 0.5-25 μm . The desirable film thickness for any given drug composition is typically determined by an

iterative process in which the desired yield and purity of the condensation aerosol composition are selected or known.

[00127] For example, if the purity of the particles is less than that which is desired, or if the percent yield is less than that which is desired, the thickness of the drug film is adjusted to a thickness different from the initial film thickness. The purity and yield are then determined at the adjusted film thickness, and this process is repeated until the desired purity and yield are achieved. After selection of an appropriate film thickness, the area of substrate required to provide a therapeutically effective dose is determined.

[00128] Generally, the film thickness for a given drug composition is such that drug-aerosol particles, formed by vaporizing the drug composition by heating the substrate and entraining the vapor in a gas stream, have (i) 10% by weight or less drug-degradation product, more preferably 5% by weight or less, most preferably 2.5% by weight or less and (ii) at least 50% of the total amount of drug composition contained in the film. The area of the substrate on which the drug composition film is formed is selected to achieve an effective human therapeutic dose of the drug aerosol as is described further below.

[00129] To determine the thickness of the drug film, one method that can be used is to determine the area of the substrate and calculate drug film thickness using the following relationship:

$$\text{film thickness (cm)} = \text{drug mass (g)} / [\text{drug density (g/cm}^3\text{)} \times \text{substrate area (cm}^2\text{)}]$$

[00130] The drug mass can be determined by weighing the substrate before and after formation of the drug film or by extracting the drug and measuring the amount analytically. Drug density can be experimentally determined by a variety of techniques, known by those of skill in the art or found in the literature or in reference texts, such as in the CRC. An assumption of unit density is acceptable if an actual drug density is not known.

[00131] The substrate having a drug film of known thickness was heated to a temperature sufficient to generate a thermal vapor. All or a portion of the thermal vapor was recovered and analyzed for presence of drug-degradation products, to determine purity of the aerosol particles in the thermal vapor. There is a clear relationship between film thickness and aerosol particle purity, whereas the film thickness decreases, the purity increases.

[00132] In addition to selection of a drug film thickness that provides aerosol particles containing 10% or less drug-degradation product (i.e., an aerosol particle purity of 90% or

more), the film thickness is selected such that at least about 50% of the total amount of drug composition contained in the film is vaporized when the substrate is heated to a temperature sufficient to vaporize the film.

[00133] To obtain higher purity aerosols one can coat a lesser amount of drug, yielding a thinner film to heat, or alternatively use the same amount of drug but a larger surface area. Generally, except for, as discussed above, extremely thin thickness of drug film, a linear decrease in film thickness is associated with a linear decrease in impurities.

[00134] Thus for the drug composition where the aerosol exhibits an increasing level of drug degradation products with increasing film thicknesses, particularly at a thickness of greater than 0.05-30 microns, the film thickness on the substrate will typically be between 0.05 and 30 microns, e.g., the maximum or near-maximum thickness within this range that allows formation of a particle aerosol with drug degradation less than 5%.

[00135] Another approach contemplates generation of drug-aerosol particles having a desired level of drug composition purity by forming the thermal vapor under a controlled atmosphere of an inert gas, such as argon, nitrogen, helium, and the like.

[00136] Once a desired purity and yield have been achieved or can be estimated from a graph of aerosol purity versus film thickness and the corresponding film thickness determined, the area of substrate required to provide a therapeutically effective dose is determined.

Substrate Area

[00137] As noted above, the surface area of the substrate surface area is selected such that it is sufficient to yield a therapeutically effective dose. The amount of drug to provide a therapeutic dose is generally known in the art and is discussed more below. The required dosage and selected film thickness, discussed above, dictate the minimum required substrate area in accord with the following relationship:

$$\text{film thickness (cm)} \times \text{drug density (g/cm}^3\text{)} \times \text{substrate area (cm}^2\text{)} = \text{dose (g)}$$

OR

$$\text{Substrate area (cm}^2\text{)} = \text{dose (g)} / [\text{film thickness (cm)} \times \text{drug density (g/cm}^3\text{)}]$$

[00138] The drug mass can be determined by weighing the substrate before and after formation of the drug film or by extracting the drug and measuring the amount analytically.

Drug density can be determined experimentally by a variety of well-known techniques, or may be found in the literature or in reference texts, such as in the CRC. An assumption of unit density is acceptable if an actual drug density is not known.

[00139] To prepare a drug supply article comprised of a drug film on a heat-conductive substrate that is capable of administering an effective human therapeutic dose, the minimum substrate surface area is determined using the relationships described above to determine a substrate area for a selected film thickness that will yield a therapeutic dose of drug aerosol.

[00140] In some variations, the selected substrate surface area is between about 0.05-500 cm². In others, the surface area is between about 0.05 and 300 cm². In one embodiment, the substrate surface area is between 0.05 and 0.5 cm². In one embodiment, substrate surface areas, are between 0.1 and 0.2 cm². The actual dose of drug delivered, i.e., the percent yield or percent emitted, from the drug-supply article will depend on, along with other factors, the percent of drug film that is vaporized upon heating the substrate. Thus, for drug films that yield upon heating 100% of the drug film and aerosol particles that have a 100% drug purity, the relationship between dose, thickness, and area given above correlates directly to the dose provided to the user. As the percent yield and/or particle purity decrease, adjustments in the substrate area can be made as needed to provide the desired dose. Also, as one of skill in the art will recognize, larger substrate areas other than the minimum calculated area for a particular film thickness can be used to deliver a therapeutically effective dose of the drug. Moreover as can be appreciated by one of skill in art, the film need not coat the complete surface area if a selected surface area exceeds the minimum required for delivering a therapeutic dose from a selected film thickness.

Dosage of Drug Containing Aerosols

[00141] The dose of a drug delivered in the aerosol refers to a unit dose amount that is generated by heating of the drug under defined conditions, cooling the ensuing vapor, and delivering the resultant aerosol. A “unit dose amount” is the total amount of drug in a given volume of inhaled aerosol. The unit dose amount may be determined by collecting the aerosol and analyzing its composition as described herein, and comparing the results of analysis of the aerosol to those of a series of reference standards containing known amounts of the drug. The amount of drug or drugs required in the starting composition for delivery as an aerosol depends on the amount of drug or drugs entering the thermal vapor phase when heated (i.e., the dose produced by the starting drug or drugs), the bioavailability of the aerosol

drug or drugs, the volume of patient inhalation, and the potency of the aerosol drug or drugs as a function of plasma drug concentration.

[00142] One can determine the appropriate dose of a drug-containing aerosol to treat a particular condition using methods such as animal experiments and a dose-finding (Phase I/II) clinical trial. These experiments may also be used to evaluate possible pulmonary toxicity of the aerosol. One animal experiment involves measuring plasma concentrations of drug in an animal after its exposure to the aerosol. Mammals such as dogs or primates are typically used in such studies, since their respiratory systems are similar to that of a human and they typically provide accurate extrapolation of test results to humans. Initial dose levels for testing in humans are generally less than or equal to the dose in the mammal model that resulted in plasma drug levels associated with a therapeutic effect in humans. Dose escalation in humans is then performed, until either an optimal therapeutic response is obtained or a dose-limiting toxicity is encountered. The actual effective amount of drug for a particular patient can vary according to the specific drug or combination thereof being utilized, the particular composition formulated, the mode of administration and the age, weight, and condition of the patient and severity of the episode being treated.

Particle Size

[00143] Efficient aerosol delivery to the lungs requires that the particles have certain penetration and settling or diffusional characteristics. Deposition in the deep lungs occurs by gravitational settling and requires particles to have an effective settling size, defined as mass median aerodynamic diameter (MMAD), typically between 1-3.5 μm . For smaller particles, deposition to the deep lung occurs by a diffusional process that requires having a particle size in the 10-100 nm, typically 20-100 nm range. An inhalation drug-delivery device for deep lung delivery should produce an aerosol having particles in one of these two size ranges, preferably between about 0.1-3 μm MMAD. Typically, in order to produce particles having a desired MMAD, gas or air is passed over the solid support at a certain flow rate.

[00144] During the condensation stage the MMAD of the aerosol is increasing over time. Typically, in variations of the invention, the MMAD increases within the size range of 0.01-3 microns as the vapor condenses as it cools by contact with the carrier gas then further increases as the aerosol particles collide with each other and coagulate into larger particles. Most typically, the MMAD grows from <0.5 micron to > 1 micron in less than 1 second. Thus typically, immediately after condensing into particles, the condensation aerosol MMAD

doubles at least once per second, often at least 2, 4, 8, or 20 times per second. In other variations, the MMAD increases within the size range of 0.1-3 microns.

[00145] Typically, the higher the flow rate, the smaller the particles that are formed. Therefore, in order to achieve smaller or larger particles, the flow rate through the condensation region of the delivery device may be altered. A desired particle size is achieved by mixing a compound in its vapor-state into a volume of a carrier gas, in a ratio such that the desired particle size is achieved when the number concentration of the mixture reaches approximately 10^9 particles/mL. The particle growth at this number concentration is then slow enough to consider the particle size to be “stable” in the context of a single deep inhalation. This may be done, for example, by modifying a gas-flow control valve to increase or decrease the volumetric airflow rate. To illustrate, condensation particles in the size range 0.1-3 μm MMAD may be produced by selecting the gas-flow rate over the vaporizing drug to be in a range of 1-10 L/minute, preferably in the range of 2-8 L/min.

[00146] Additionally, as will be appreciated by one of skill in the art, particle size may also be altered by modifying the cross-section of the chamber condensation region to increase or decrease linear gas velocity for a given volumetric flow rate. In addition, particle size may also be altered by the presence or absence of structures that produce turbulence within the chamber. Thus, for example to produce condensation particles in the size range 10-100 nm MMAD, the chamber may provide gas-flow barriers for creating air turbulence within the condensation chamber. These barriers are typically placed within a few thousandths of an inch from the substrate surface.

Analysis of Drug Containing Aerosols

[00147] Purity of a drug-containing aerosol may be determined using a number of different methods. It should be noted that when the term “purity” is used, it refers to the percentage of aerosol minus the percent byproduct produced in its formation. Byproducts for example, are those unwanted products produced during vaporization. For example, byproducts include thermal degradation products as well as any unwanted metabolites of the active compound or compounds. Examples of suitable methods for determining aerosol purity are described in Sekine *et al.*, *Journal of Forensic Science* 32:1271-1280 (1987) and in Martin *et al.*, *Journal of Analytic Toxicology* 13:158-162 (1989).

[00148] One suitable method involves the use of a trap. In this method, the aerosol is collected in a trap in order to determine the percent or fraction of byproduct. Any suitable

trap may be used. Suitable traps include filters, glass wool, impingers, solvent traps, cold traps, and the like. Filters are often most desirable. The trap is then typically extracted with a solvent, *e.g.* acetonitrile, and the extract subjected to analysis by any of a variety of analytical methods known in the art, for example, gas, liquid, and high performance liquid chromatography particularly useful.

[00149] The gas or liquid chromatography method typically includes a detector system, such as a mass spectrometry detector or an ultraviolet absorption detector. Ideally, the detector system allows determination of the quantity of the components of the drug composition and of the byproduct, by weight. This is achieved in practice by measuring the signal obtained upon analysis of one or more known mass(es) of components of the drug composition or byproduct (standards) and then comparing the signal obtained upon analysis of the aerosol to that obtained upon analysis of the standard(s), an approach well known in the art.

[00150] In many cases, the structure of a byproduct may not be known or a standard for it may not be available. In such cases, one may calculate the weight fraction of the byproduct by assuming it has an identical response coefficient (*e.g.* for ultraviolet absorption detection, identical extinction coefficient) to the drug component or components in the drug composition. When conducting such analysis, byproducts present in less than a very small fraction of the drug compound, *e.g.* less than 0.1% or 0.03% of the drug compound, are typically excluded. Because of the frequent necessity to assume an identical response coefficient between drug and byproduct in calculating a weight percentage of byproduct, it is often more desirable to use an analytical approach in which such an assumption has a high probability of validity. In this respect, high performance liquid chromatography with detection by absorption of ultraviolet light at 225 nm is typically desirable. UV absorption at 250 nm may be used for detection of compounds in cases where the compound absorbs more strongly at 250 nm or for other reasons one skilled in the art would consider detection at 250 nm the most appropriate means of estimating purity by weight using HPLC analysis. In certain cases where analysis of the drug by UV are not viable, other analytical tools such as GC/MS or LC/MS may be used to determine purity.

[00151] It is possible that changing the gas under which vaporization of the composition occurs may also impact the purity.

Other Analytical Methods

[00152] Particle size distribution of a drug-containing aerosol may be determined using any suitable method in the art (*e.g.*, cascade impaction). A Next Generation Cascade Impactor (MSP Corporation, Shoreview, MN) linked to a vaporization device by an induction port (USP induction port, MSP Corporation, Shoreview, MN) is one system used for cascade impaction studies.

[00153] Inhalable aerosol mass density may be determined, for example, by delivering a drug-containing aerosol into a confined chamber via an inhalation device and measuring the mass collected in the chamber. Typically, the aerosol is drawn into the chamber by having a pressure gradient between the device and the chamber, wherein the chamber is at lower pressure than the device. The volume of the chamber should approximate the inhalation volume of an inhaling patient, typically about 2-4 liters.

[00154] Inhalable aerosol drug mass density may be determined, for example, by delivering a drug-containing aerosol into a confined chamber via an inhalation device and measuring the amount of active drug compound collected in the chamber. Typically, the aerosol is drawn into the chamber by having a pressure gradient between the device and the chamber, wherein the chamber is at lower pressure than the device. The volume of the chamber should approximate the inhalation volume of an inhaling patient, typically about 2-4 liters. The amount of active drug compound collected in the chamber is determined by extracting the chamber, conducting chromatographic analysis of the extract and comparing the results of the chromatographic analysis to those of a standard containing known amounts of drug.

[00155] Inhalable aerosol particle concentration may be determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device and measuring the number of particles of given size collected in the chamber. The number of particles of a given size may be directly measured based on the light-scattering properties of the particles. Alternatively, the number of particles of a given size may be determined by measuring the mass of particles within the given size range and calculating the number of particles based on the mass as follows: Total number of particles = Sum (from size range 1 to size range N) of number of particles in each size range. Number of particles in a given size range = Mass in the size range/Mass of a typical particle in the size range. Mass of a typical particle in a given size range = $\pi \cdot D^3 \cdot \phi / 6$, where D is a typical particle diameter in the size

range (generally, the mean boundary MMADs defining the size range) in microns, ϕ is the particle density (in g/mL) and mass is given in units of picograms (g^{-12}).

[00156] Rate of inhalable aerosol particle formation may be determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device. The delivery is for a set period of time (*e.g.*, 3 s), and the number of particles of a given size collected in the chamber is determined as outlined above. The rate of particle formation is equal to the number of 10 nm to 5 micron particles collected divided by the duration of the collection time.

[00157] Rate of aerosol formation may be determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device. The delivery is for a set period of time (*e.g.*, 3 s), and the mass of particulate matter collected is determined by weighing the confined chamber before and after the delivery of the particulate matter. The rate of aerosol formation is equal to the increase in mass in the chamber divided by the duration of the collection time. Alternatively, where a change in mass of the delivery device or component thereof can only occur through release of the aerosol phase particulate matter, the mass of particulate matter may be equated with the mass lost from the device or component during the delivery of the aerosol. In this case, the rate of aerosol formation is equal to the decrease in mass of the device or component during the delivery event divided by the duration of the delivery event.

[00158] Rate of drug aerosol formation may be determined, for example, by delivering a drug-containing aerosol into a confined chamber via an inhalation device over a set period of time (*e.g.*, 3 s). Where the aerosol is a pure drug, the amount of drug collected in the chamber is measured as described above. The rate of drug aerosol formation is equal to the amount of drug collected in the chamber divided by the duration of the collection time. Where the drug-containing aerosol comprises a pharmaceutically acceptable excipient, multiplying the rate of aerosol formation by the percentage of drug in the aerosol provides the rate of drug aerosol formation.

Kits

[00159] In an embodiment of the invention, a kit is provided for use by a healthcare provider, or more preferably a patient. The kit for delivering a condensation aerosol typically comprises a composition comprising a drug, and a device for forming a condensation aerosol. The composition is typically void of solvents and excipients and generally comprises a heat

stable drug. The device for forming a condensation aerosol typically comprises an element configured to heat the composition to form a vapor, an element allowing the vapor to condense to form a condensation aerosol, and an element permitting a user to inhale the condensation aerosol. The device in the kit may further comprise features such as breath-actuation or lockout elements or dose counting/logging or tapering devices. An exemplary kit will provide a hand-held aerosol delivery device and at least one dose.

[00160] In another embodiment, kits for delivering a nicotine aerosol comprising a thin film of nicotine meta-salicylate composition and a device for dispensing said film as a condensation aerosol are provided. The composition may contain pharmaceutical excipients. The device for dispensing said film of a drug composition as an aerosol comprises an element configured to heat the film to form a vapor, and an element allowing the vapor to condense to form a condensation aerosol.

[00161] In the kits of the invention, the composition is typically coated as a thin film, generally at a thickness between about 0.5-30 microns, on a substrate which is heated by a heat source. Heat sources typically supply heat to the substrate at a rate that achieves a substrate temperature of at least 200° C, preferably at least 250 °C, or more preferably at least 300 °C or 350 °C, and produces substantially complete volatilization of the drug composition from the substrate within a period of 2 seconds, preferably, within 1 second, or more preferably within 0.5 seconds. To prevent drug degradation, it is preferable that the heat source does not heat the substrate to temperature greater than 600 °C while the drug film is on the substrate to prevent. More preferably, the heat source does not heat the substrate in to temperatures in excess of 500 °C.

[00162] The kit of the invention can be comprised of various combinations of nicotine and drug delivery devices. In some embodiments the device may also be present with another drug. The other drug may be administered orally or topically. Generally, instructions for use are included in the kits.

[00163] In certain embodiments, thin films of nicotine meta-salicylate can be used to provide multiple doses of nicotine provided on a spool or reel of tape. For example, a tape can comprise a plurality of drug supply units with each drug supply unit comprising a heat package on which a thin film comprising nicotine meta-salicylate is disposed. Each heat package can include an initiator composition that can be ignited, for example, by resistive heating or percussively, and a fuel capable of providing a rapid, high temperature heat impulse sufficient to selectively vaporize the nicotine meta-salicylate. Each heat package can

be spaced at intervals along the length of the tape. During use, one or more heat packages can be positioned within an airway and, while air is flowing through the airway, the heat package can be activated to selectively vaporize nicotine meta-salicylate. The vaporized nicotine can condense in the air flow to form an aerosol comprising the nicotine which can then be inhaled by a user. The tape can comprise a plurality of thin films that define the regions where the initiator composition, fuel, and thin film comprising nicotine meta-salicylate are disposed. Certain of the multiple layers can further provide unfilled volume for released gases to accumulate to minimize pressure buildup. The plurality of layers can be formed from any material which can provide mechanical support and that will not appreciably chemically degrade at the temperatures reached by the heat package. In certain embodiments, a layer can comprise a metal or a polymer such as polyimide, fluoropolymer, polyetherimide, polyether ketone, polyether sulfone, polycarbonate, or other high temperature resistance polymers. In certain embodiments, the tape can further comprise an upper and lower layer configured to physically and/or environmentally protect the drug. The upper and/or lower protective layers can comprise, for example, a metal foil, a polymer, or can comprise a multilayer comprising metal foil and polymers. In certain embodiments, protective layers can exhibit low permeability to oxygen, moisture, and/or corrosive gases. All or portions of a protective layer can be removed prior to use to expose a drug and fuel. The initiator composition and fuel composition can comprise, for example, any of those disclosed herein. Thin film heat packages and drug supply units in the form of a tape, disk, or other substantially planar structure, can provide a compact and manufacturable method for providing a large number of doses of a substance. Providing a large number of doses at low cost can be particularly useful in certain therapies, such as for example, in administering nicotine for the treatment of nicotine craving and/or effecting cessation of smoking.

[00164] The disclosure provides techniques for implementing drug delivery and drug cessation control. A drug delivery system might be provided having a form factor similar to a cigarette or cigar in the case that the drug is nicotine, nicotine meta-salicylate, or other nicotine related drug. Within the cigarette or cigar -shaped drug delivery device, a coil arrangement, a foil arrangement, or a resistive contact arrangement might form a circuit path to a current source. Each coil, foil, or resistive contact might be coated with the nicotine-based drug, or might be in thermal contact with a substrate coated with the nicotine-based drug. A control device might interface wirelessly with the cigarette or cigar -shaped drug

delivery device to wirelessly control or manage delivery of the nicotine-based drug and to control cessation in the use of the drug

[00165] In certain embodiments, the disclosure teaches a drug delivery and drug cessation system, comprising: a portable control device comprising a user input device, a first wireless transceiver, a second wireless transceiver, a processor, a memory device, and a network interface device; a drug delivery device comprising a third wireless transceiver, a dosage control device, a drug payload, and a dosage delivery device; and one or more user sensors each in contact with a portion of a body of a user, each of the one or more user sensors comprising a fourth wireless transceiver and one or more measurement sensors, the one or more measurement sensors comprising one or more of an oximeter, a pulse measurement sensor, a respiration rate sensor, or a blood pressure sensor. The user input device receives user inputs from the user to control drug delivery to the body of the user and to control drug cessation; the drug payload comprises a reservoir configured to contain amounts of a drug sufficient for one or more doses; the processor communicates with the drug delivery device via the first and third wireless transceivers to send first instructions to the dosage control device based on one or more of the user inputs, one or more preset instructions associated with drug delivery and drug cessation, or one or more measurement results from the one or more measurement sensors that are transmitted to the portable control device via the second and fourth wireless transceivers; the dosage control device determines an amount of the drug to be prepared for each dose based on the first instructions from the processor, and sends second instructions to the dosage delivery device to prepare and deliver the determined amount of the drug for delivery for each dose; the dosage delivery device delivers the drug from the drug payload to the user based on the second instructions from the dosage control device; the memory device stores a history of drug delivery using the system, the history of drug delivery comprising one or more of the one or more measurement results prior to each dose, drug dosages for each predetermined period, increases in drug dosage, decreases in drug dosage, number of doses for each predetermined period, increases in number of doses for each predetermined period, decreases in number of doses for each predetermined period, number of user-initiated drug delivery overrides, types of user-initiated drug delivery overrides, or contact information of a physician associated with the user; and the network interface communicatively couples with a computing device of the physician over a network to send the history of drug delivery to the physician and to receive drug dosage prescriptions from the physician.

[00166] The disclosure further teaches a drug delivery and drug cessation system, comprising: a portable drug delivery device comprising a drug payload, a dosage delivery device, and a first wireless transceiver; a portable control device comprising a second wireless transceiver, the portable control device being in wireless communication with the portable drug delivery device via the first wireless transceiver and the second wireless transceiver; the portable drug delivery device being configured to deliver a drug to a body of a user based on instructions received from the portable control device. The drug delivery device can be further characterized wherein the portable drug delivery device is a vapor-based drug delivery device.

[00167] The disclosure further teaches a drug delivery and drug cessation system, wherein the portable drug delivery device further comprises a breath actuator and a lockout unit, wherein the breath actuator is configured to cause the dosage delivery device to deliver a supplemental dose of the drug from the drug payload, based on a determination that the user has inhaled from the portable drug delivery device, and wherein the lockout unit is configured to prevent the breath actuator from causing the dosage delivery device to deliver the supplemental dose of the drug during a predetermined period based on a determination that the supplemental dose would exceed a predetermined maximum dose of the drug for the predetermined period.

[00168] The drug delivery and drug cessation system may be further characterized, wherein the breath actuator is configured to cause the dosage delivery device to deliver the supplemental dose of the drug from the drug payload, based on a determination that the user has inhaled from the portable drug delivery device, without receiving the instructions from the portable control device and contrary to any preset dosage schedule.

[00169] The drug delivery and drug cessation system may be further characterized, wherein the drug payload comprises one or more foils coated with the drug, wherein the dosage delivery device comprises a heater configured to heat one of a portion of each foil or an entire surface of each foil to at least 200 degrees Celsius within less than 2 seconds.

[00170] The drug delivery and drug cessation system may be further characterized wherein the heater is configured to heat one of a portion of each foil or an entire surface of each foil to at least 300 degrees Celsius within less than 0.5 seconds.

[00171] The drug delivery and drug cessation system may be further characterized, wherein the drug payload comprises a plurality of resistive coils connected in series and a plurality of fuses connected to a ground wire, each fuse separating each coil from a next

adjacent coil in the series, wherein each of the plurality of coils is coated with the drug, wherein the dosage delivery device comprises a current source configured to heat each coil to at least 200 degrees Celsius within less than 2 seconds, wherein a circuit path is established from the current source to the plurality of coils in the series to the ground wire, with each fuse defining a short-circuit path between each coil and the next adjacent coil in the series, and wherein the current source is further configured to send a short current burst to cause an unfailed fuse closest to the current source to fail, thereby allowing the next adjacent coil in the series to be energized by the current source.

[00172] The drug delivery and drug cessation system may be further characterized, wherein the drug payload comprises a thin film structure comprising a plurality of foils connected in series and a plurality of fuses connected to a ground portion of the thin film structure, each fuse separating each foil from a next adjacent foil in the series, wherein each of the plurality of foils is coated with the drug, wherein the dosage delivery device comprises a current source configured to heat each foil to at least 200 degrees Celsius within less than 2 seconds, wherein a circuit path is established from the current source to the plurality of foils in the series to the ground wire, with each fuse defining a short-circuit path between each foil and the next adjacent foil in the series, and wherein the current source is further configured to send a short current burst to cause an unfailed fuse closest to the current source to fail, thereby allowing the next adjacent foil in the series to be energized by the current source.

[00173] The drug delivery and drug cessation system may be further characterized, wherein the thin film structure has an overall shape of one of a flat foil wrapped in wedge form, a flat foil wrapped in tubular form, or a planar structure.

[00174] The drug delivery and drug cessation system may be further characterized, wherein the portable drug delivery device is a transdermal-based drug delivery device.

[00175] The drug delivery and drug cessation system may be further characterized, wherein the drug payload comprises a liquid reservoir containing the drug in liquid form, wherein the dosage delivery device comprises a variable permeability membrane and a membrane actuator, said variable permeability membrane configured to change liquid permeability so as to deliver varying amounts of the drug from the liquid reservoir, based on control signals from the membrane actuator.

[00176] The drug delivery and drug cessation system may be further characterized, wherein the drug payload comprises a plurality of foils arranged in a first grid comprising a first plurality of rows and a first plurality of columns, each foil being coated with the drug

and each foil being separated from each other by electrically and thermally non-conductive material, wherein the dosage delivery device comprises a first group of switches, a second group of switches, a current source electrically coupled to each of the first group of switches, an electrical ground path electrically coupled to each of the second group of switches, a plurality of actuators arranged in a second grid comprising a second plurality of rows and a second plurality of columns, a first plurality of linear electrical paths, a second plurality of linear electrical paths, wherein for each column in the second plurality of columns, a first electrical path is established from one of the first group of switches to each of the plurality of actuators arranged in the subject column in the second plurality of columns, wherein for each row in the second plurality of rows, a second electrical path is established from one of the second group of switches to each of the plurality of actuators arranged in the subject column in the second plurality of rows, wherein the plurality of foils arranged in the first grid is aligned with the plurality of actuators arranged in the second grid so as to make direct contact therewith.

[00177] The drug delivery and drug cessation system may be further characterized, wherein each of the plurality of actuators includes a resistive element configured to reach a temperature of at least 200 degrees Celsius within less than 2 seconds with application of a predetermined amount of current, wherein each of the plurality of foils arranged in the first grid is individually heated by closing one of the first group of switches and closing one of the second group of switches, thereby energizing a subject resistive element electrically coupled to both the one of the first group of switches and the one of the second group of switches, in turn heating a subject foil of the plurality of foils that is in direct contact with the subject resistive element.

[00178] The drug delivery and drug cessation system of may be further characterized, wherein the dosage delivery device further comprises a membrane in physical contact with the body of the user, wherein the drug heated by the subject foil flows as one of a gas or a liquid through the membrane to be absorbed by a skin portion of the body of the user.

[00179] The drug delivery and drug cessation system may be further characterized, wherein each switch in the first and second group of switches is a transistor.

[00180] The disclosure teaches a drug delivery and drug cessation system further comprising: one or more user sensors each in contact with a portion of the body of the user, each of the one or more user sensors comprising a third wireless transceiver and one or more measurement sensors, the one or more measurement sensors comprising one or more of an

oximeter, a pulse measurement sensor, a respiration rate sensor, or a blood pressure sensor, wherein the portable drug delivery device is configured to deliver the drug to the body of the user based on instructions received from the portable control device and based on measurement results received from the one or more measurement sensors via the third wireless transceiver.

[00181] The disclosure teaches a drug delivery and drug cessation system, wherein the portable control device further comprises a memory device and a network interface, wherein the memory device is configured to store a history of drug delivery using the system, the history of drug delivery comprising one or more of drug dosages for each predetermined period, increases in drug dosage, decreases in drug dosage, number of doses for each predetermined period, increases in number of doses for each predetermined period, decreases in number of doses for each predetermined period, number of user-initiated drug delivery overrides, types of user-initiated drug delivery overrides, or contact information of a healthcare professional associated with the user, wherein the network interface communicatively couples with a computing device of the healthcare professional over a network to send the history of drug delivery to the healthcare professional and to receive drug dosage prescriptions from the healthcare professional.

[00182] The disclosure teaches a drug delivery and drug cessation method, comprising: providing a drug delivery and drug cessation system, comprising: a portable drug delivery device comprising a drug payload, a dosage delivery device, and a first wireless transceiver; and a portable control device comprising a second wireless transceiver, the portable control device being in wireless communication with the portable drug delivery device via the first wireless transceiver and the second wireless transceiver; delivering, by the portable drug delivery device, a dose of a drug stored in the drug payload to a body of a user based on first instructions received from the portable control device.

[00183] The drug delivery and drug cessation method may be further characterized, comprising: receiving, at the portable control device, second instructions comprising at least one of instructions based on user input, instructions based on preset dosages, or instructions from a healthcare professional via a computing device of the healthcare professional over a network, wherein the first instructions are based on the second instructions; and receiving, at the portable drug delivery device, the first instructions from the portable control device.

[00184] The disclosure teaches a drug delivery and drug cessation apparatus, comprising: a processor; and a non-transitory computer readable medium having stored

thereon computer software comprising a set of instructions that, when executed by the processor, causes the apparatus to perform one or more functions, the set of instructions comprising: instructions to deliver, by a portable drug delivery device comprising a drug payload, a dosage delivery device, and a first wireless transceiver, a dose of a drug stored in the drug payload to a body of a user based on first instructions received from a portable control device comprising a second wireless transceiver, the portable control device being in wireless communication with the portable drug delivery device via the first wireless transceiver and the second wireless transceiver.

[00185] The drug delivery and drug cessation apparatus may be further characterized, wherein the set of instructions further comprises: instructions to receive a first set of dosage instructions comprising at least one of dosage instructions based on user input, dosage instructions based on preset dosages, or dosage instructions from a healthcare professional via a computing device of the healthcare professional over a network; and instructions to receive, at the portable drug delivery device, the first instructions from the portable control device.

[00186] Various embodiments of the disclosure could also include permutations of the various elements recited in the claims as if each dependent claim was a multiple dependent claim incorporating the limitations of each of the preceding dependent claims as well as the independent claims. Such permutations are expressly within the scope of this disclosure.

[00187] While the invention has been particularly shown and described with reference to a number of embodiments, it would be understood by those skilled in the art that changes in the form and details may be made to the various embodiments disclosed herein without departing from the spirit and scope of the invention and that the various embodiments disclosed herein are not intended to act as limitations on the scope of the claims. All references cited herein are incorporated in their entirety by reference.

EXAMPLES

[00188] The following examples are provided for illustrative purposes only and are not intended to limit the scope of the invention.

Example 1

[00189] Synthesis of nicotine meta-salicylate: 1.385 g m-salicylic acid (Sigma Aldrich) was dissolved in 25 ml of ethanol. 1.62 g nicotine was added drop wise at room temperature

and mixed well for approx. 30 minutes. The solution was rotary evaporated slowly to reduce the volume to about 10 ml. Then 5 ml of ethyl acetate was added and stirred for 3-5 minutes. The solution was placed on dry ice for approx. 1.5 hours, which produced a sticky solid material. After evaporation of the solvent, 20 mL ethanol was added to dissolve the sticky solid and then evaporated. This recrystallization is known in the art for purifying crystals. Crystalline solid remained in the flask. The powder was removed from the flask and dried in a vacuum oven at 40°C. 2.6 grams were recovered (approx. 87% yield). The melting point of the solid was 125°C.

Example 2

[00190] Synthesis of nicotine meta-salicylate: Liquid Nicotine (Alfa Aesar, lot#10150504, purity 99%) and m-salicylic acid (3- hydrobenzoic acid, Sigma Aldrich, lot#STBB7747, purity 99%) were used to synthesize nicotine m-salicylate at a 1:1 nicotine:acid ratio. The following synthetic route leads to typical yields of 60-70% and purity 99.7%.

Sample synthesis:

1. Dissolved 0.03 moles of m-salicylic acid (~4.16 g) in 65 ml of ethanol 200 proof, and mixed well for about 20 min.
2. Added 0.03 moles of liquid nicotine (~4.86 g) to above solution dropwise, mixed for 30-40 min on stir plate with periodic shaking. Seed crystals of nicotine m-salicylate were then added and the solution stirred for another 40 min, then placed on dry ice for about 40 min.
3. Filtered and washed nicotine m-salicylate with 100% acetone and let it air dry for ~20 min; to homogenize the salt, a mortar and pestle were used and then the salt was dried in a vacuum oven at 40°C for 1 hour.
4. Salt was transferred into a scintillation vial and weighed. 6.0 g were recovered (~67% yield). The salt is a white powder with melting point of 125°C. Note that in the very first synthesis of this material (before there were seed crystals to utilize), after step 2 (dropwise addition of nicotine) the solution was rotary evaporated slowly to reduce to ~10 ml volume. Then 50 ml of ethyl acetate was added, mixed well, and the solution placed on dry ice. A sticky material resulted, which was further evaporated. 20 ml of ethanol was added, the solution placed again on dry ice, at which point

crystallization occurred. The crystals were filtered, washed and dried under vacuum at 40°C.

Example 3:

API Assessment:

[00191] The nicotine m-salicylate raw material (API) was characterized with a number of analytical methods. The results prove that the nicotine m-salicylate as synthesized is highly pure.

[00192] A typical calorimetric scan of nicotine m-salicylate powder is illustrated in Figure 2. The melting point is 125°C. Thermogravimetric analysis on the powder was run in both scanning and isothermal modes. Figure 7 shows the scanning data, from room temperature to 500°C. Note the flat baseline near (actually, slightly below) 0%, indicating little to no residue left behind. The pan was weighed before and after on an external balance, and the residual was only ~0.2%. This result suggests minimal charring of the acid after exposure to high temperatures. Isothermal data were also obtained on the API powder (~10 mg per run) at 40°C, 50°C, and 60°C for periods of at least 3 days. In all cases, the mass change was essentially a linear decrease with time. A summary of the data, along with similar data obtained for various other nicotine salts, is detailed in Table 1. Nicotine meta-salicylate (top line) lost about 2-3X less nicotine than nicotine ortho-salicylate (second line). Most of the nicotine salts tested were less stable (lost more nicotine) than the m-salicylate salt.

Table 1: Nicotine mass loss observed during thermogravimetric analysis experiments on various nicotine salts

Species	Nicotine Mass Loss (mcg/day)		
	40°C	50°C	60°C
Nicotine m-salicylate	5	19	107
Nicotine o-salicylate	15	48	178
Nicotine bitartrate	1	3	10
Nicotine monofumarate	7	39	219
Nicotine bifumarate	12	66	305
Nicotine bidimethylmalonate	4	14	53
Nicotine monodimethylmalonate	51	374	2707

Example 4:

Solubility

[00193] Solubility limit tests were performed on nicotine m-salicylate in a number of relevant solvents. Results are compiled in Table 2. The approximate saturation limits are in units of mg nicotine equivalent per mL of solvent. Note the solubility of nicotine m-salicylate is low in pure acetonitrile (~10 mg/mL) and acetone (< 10 mg/mL). Nicotine m-salicylate is most soluble in solvent systems containing methanol. However, the analytical methods developed for detecting impurities related to the m-salicylate use 236 nm as the detection wavelength. Methanol has high absorbance in this range and can therefore interfere with the analytes of interest. Acetonitrile, on the other hand, has low background absorbance in this wavelength range and is therefore ideal for use. To counter the poor solubility, extractions use mixtures of water and acetonitrile.

Table 2: Approximate Solubility Limits of Nicotine m-salicylate in Various Solvents

Solvent	Saturation point (mg nicotine/mL)
Acetonitrile	9
Ethanol	33
Water	58
50/50 acetonitrile/water	64
80/20 methanol/water	118
Acetone	<<10
Methanol	103

Example 5

Nicotine Coating Development

[00194] Spray coating is one of the key manufacturing steps for producing the drug films that lead to condensation aerosols. Spray coating of nicotine m-salicylate was done with solutions of ~75 mg/mL in methanol. Acetone was also tried, but the solubility was limited. Typical spray coating parameters were 1.3 W (Broadband Ultrasonic Generator power), solution flow rate 10-12 mL/hr, coating table speed 25 mm/s, and air pressure 1-1.5 psi. Higher flow rates tend to lead to visibly more heterogeneous coatings. Intra-array relative

standard deviations were often in the 2-3% range, though inter-array variability was higher (likely due to overspray onto neighboring arrays). Crystallization of the coated films is preferable, and usually occurs quite readily after manual seeding of the spray nozzle.

[00195] Coatings were made such that the 200 µg nicotine equivalent dose covers one surface of the foil, in a 9 x 2 mm area. This is equivalent to a film thickness of approximately 20 µm. Lower dosages were coated over the same surface area, for the characterization studies described below. However, as the mechanical stability of the highest dose was found to be acceptable, and the evaporative loss is less for thicker films, the disclosure teaches coating at the 20 µm thickness. New spray coating masks have been made to produce such films, at doses of 25, 50, and 100 µg nicotine equivalent.

Example 6

Analytical Method Development

[00196] In conjunction with the drug product development of nicotine m-salicylate, a number of analytical methods have been derived to assist with the quantitative and qualitative (purity) assessment of the API and the aerosol.

[00197] Nicotine quantitative: This isocratic assay uses a Gemini C18, 50 x 3.0 mm, 3 µm column, 0.1% ammonium hydroxide in water/acetonitrile mobile phase with flow rate of 0.6 mL/min and detection at 245 nm. The total run time for this method is 3 minutes. This procedure is applicable for determining nicotine concentrations in the range of 8 to 200 µg/mL for low quant and 100 to 600 µg/mL for high quant in nicotine salts. It is not intended for the measurement of impurities or degradants of nicotine.

[00198] M-salicylic acid quantitative method: This isocratic assay uses a Luna, C18, 3 µm, 75 x 4.6 mm column, 0.1% trifluoroacetic acid (TFA) in water/acetonitrile mobile phase with flow rate of 1.0 mL/min and detection at 248nm. The total run time for this method is 3.5 minutes. This procedure is applicable for determining m-salicylic acid concentrations in the range of 20 to 600 µg/mL. It is not intended for the measurement of impurities or degradants of m-salicylic acid.

[00199] Nicotine purity method: This reverse phase HPLC method applies a gradient flow with a mobile phase composed of 0.1% (v/v) ammonium hydroxide in water/acetonitrile at a flow rate of 0.8 mL/min, and uses a Gemini RP18, 150 x 4.6 mm, 3 µm column, and UV detection at 260 nm. The total run time for this method is 20 minutes. This procedure is applicable for determining nicotine concentrations and the nicotine related impurities in a

nicotine concentration range of 300 to 500 µg/mL. It is for the determination of the total nicotine-related impurities in nicotine m-salicylate.

[00200] M-salicylic acid purity method (AARD-020-049): This reverse phase HPLC method applies a gradient flow with a mobile phase composed of 0.1% (v/v) trifluoroacetic acid (TFA) in water/acetonitrile at a flow rate of 0.8 mL/min, and uses a Gemini C18, 150 x 3.0 mm, 5 µm column, and UV detection at 236 nm. The total run time for this method is 20 minutes. This procedure is applicable for determining m-salicylate concentrations and the m-salicylate related impurities in an m-salicylate concentration range of 300 to 500 µg/mL. It is for the determination of the total m-salicylic acid-related impurities in nicotine m-salicylate.

Example 7

EMD Characterization

Emitted Dose and Mass Balance

[00201] Emitted Dose and Mass Balance: Due to the volatile nature of nicotine, a thorough collection of nicotine particles and vapors proved to be extremely challenging. Many iterations of emitted dose testing were performed to find the optimal collection method that enabled 100% mass balance.

[00202] Ultimately, a 76 mm diameter glass fiber filter (1.0 µm pore size, type A/E), housed in the NGI filter holder, was found to provide the optimal recovery of both nicotine and the m-salicylate. Possibly the nicotine salicylate salts require a relatively slow face velocity across the filter for adequate collection. Emitted dose experiments were conducted using a switch box with external power supply to provide the energy to heat up the foils and vaporize the drug. Up to 3 foils can be fired into one filter without negatively impacting recovery. (Actuating more foils into one filter decreases aerosol recovery, possibly due to the volatility of free base nicotine from the extra air flow across the collection filter.) The switch box was set to provide 3.7 volts/4.0 amps for 0.5 seconds. Airflow rate was set at 28.3 LPM. The captured drug vapors were then extracted from the filter using up to 10 mL of 50% (v/v) acetonitrile in water and sonicated for 10 minutes. Filter fibers are pelleted out by centrifugation before the analyte is prepared for HPLC analysis.

[00203] The average nicotine emitted dose from foils coated with 200 µg nicotine was 99.5% of coated dose (6.8% SD) while the average m-salicylate recovery was 101.8% compared to coated dose (6.3% SD). Both had minimal deposition/residual on the foils and airway housing. Additionally, an analysis of the nicotine to counter-ion molar ratios for both

the coated dose and emitted dose results show that the 1:1 relationship is conserved during the vaporization and capture process.

Aerosol Purity

[00204] Aerosols were captured with the emitted dose procedure, with extractions carried out in 50/50 acetonitrile/water. The purity of the aerosol is dictated by both the nicotine and the salicylate entities. The nicotine moiety appears to vaporize almost completely intact, with minimal ($\leq 0.5\%$) degradation. Small amounts of myosmine were detected. Figure 8 shows a chromatogram of a typical sample run on the nicotine impurity method.

[00205] The challenge of a number of the nicotine salts, such as the tartrate, has been the decomposition of the acid. What complicates the situation further is the analytical challenge in observing their degradation byproducts, since these carboxylic acids are small molecules with minimal UV absorption. The m-salicylate, fortunately, has some advantages in this regard. We were able to develop an HPLC method for screening degradation of m-salicylate. Minimal degradation products from m-salicylic acid have been detected ($\leq 0.5\%$). Figure 9 shows a chromatogram of a typical sample run on the m-salicylate impurity method.

[00206] An additional concern of the m-salicylic acid was the possible formation of phenol. Phenol has been detected as a decomposition product of nicotine o-salicylate at levels of ~ 0.1 - 0.5% . While phenol is a relatively ubiquitous molecule, there are some reports of genotoxicity and irritation.

[00207] Using a sensitive LC method for phenol detection, this method did not observe phenol in nicotine m-salicylate aerosols. Given the sensitivity of the method, we can estimate a maximum content of about 0.013% phenol in the nicotine m-salicylate aerosols. A complementary approach to evaluating aerosol purity is calculating the mass balance, i.e., comparing the coated dose amount to the emitted dose plus the residual amounts of nicotine and counterion. Comparing the amounts and ratio of nicotine and m-salicylic acid in the coated vs. emitted + residual drug shows that unlike the tremendous disparity seen in salts such as nicotine bitartrate, the mass balance of both entities is about 100% and the ratio in the aerosol is consistent with that of the coated dose.

Aerosol Particle Size Results

[00208] Particle size experiments were conducted on the Next Generation Impactor (NGI). Airflow rate was set at 30 LPM. Foil arrays coated with 200 μg of nicotine equivalent (about 370 g total of nicotine m-salicylate) were vaporized using an EMD dose cartridge switch box at settings similar to the emitted dose experiments. Four to eleven foils were vaporized into each NGI set and cups were assayed with 4 mL of 50% (v/v) acetonitrile in water. Initially, bare NGI cups resulted in low MMAD values, with an average of 0.7 μm . Silicone was then sprayed onto the cups to reduce the bounce effects often seen with particle size experiments. Silicone sprayed cups had no effect on MMAD, though mass balance improved slightly, increasing nicotine recovery from 76% of coated dose for bare cups to 89% on silicone cups. The NGI cups were then coated with a thin layer of 1% (w/v) benzoic acid to reduce bounce and nicotine volatility. An aliquot of the solution was pipetted into each cup, and the cups were swirled to expedite surface coverage. The presence of benzoic acid increased the MMAD to 0.9 μm , while nicotine recovery improved to 93% of coated dose. Figure 10 shows the particle size distribution amongst the various impactor stages for these setups.

[00209] Further experiments to determine effects of benzoic acid coating uniformity and thickness (by varying number of sprays from a spray bottle) showed minimal difference to the MMAD, with results ranging from 0.8 to 1.0 μm . See Figure 11. Particle size is about 1 μm , or just slightly less, which should be appropriate for pulmonary deposition. It is likely that the nicotine m-salicylate aerosols would grow somewhat in the humid (nearly 100% RH) atmosphere inside the respiratory tract.

Example 8

Stability

[00210] The innate volatility of free base nicotine can be greatly altered once bound to a counterion acid. The stability of nicotine in the resulting salt form can vary widely, ultimately impacting its desirability for commercial consideration. Certain packaging configurations can mitigate nicotine loss. Previous experimental results suggested that nicotine loss is halted once the equilibrium vapor pressure of nicotine is reached. Decreasing the equilibrium vapor pressure point is believed to minimize the total nicotine loss. For this study, different packaging configurations were tested to investigate the following variables: container material, presence of adjuncts, and total volume of space. Container materials

consisted of either glass or multi-laminate foil pouches. Glass is impermeable to vapors. Once the total volume of the glass container is flooded with nicotine vapors and any surface adsorption occurs, equilibrium is reached and no additional loss of nicotine should be observed. Though foil is also impermeable, the inner surface of the pouch is lined with an ethylene acid copolymer that promotes vapor absorbency. The copolymer should lead to greater nicotine loss within a pouch than a glass vial of the same total volume.

[00211] The presence of adjuncts, such as a drug cartridge housing, is a likely scenario for the final commercial product. The composition of the adjunct will affect equilibrium vapor pressure point if it preferentially absorbs vapors. For this study, a polycarbonate adjunct with a surface area of $\sim 150 \text{ cm}^2$ was introduced to the glass vial and pouch scenarios. Finally, the total packaging volume was examined. The smaller the available space, the sooner the equilibrium pressure can be reached. Open containers represent the worst case scenario, as the infinite space means that the equilibrium pressure can never be achieved. To set up the experiment, screening foils were spray coated with a 1 x 2cm footprint of nicotine m-salicylate to a thickness of $\sim 11 \text{ ug nicotine/mm}^2$ (equivalent to a coated dose of 200 ug nicotine equivalent on an EMD foil). After a few random screening foils were assayed for initial time point coated dose, the remaining foils were placed in one of the following containers:

- Capped glass vial ($\sim 40 \text{ mL}$ volume)
- Heat-sealed standard pouch ($\sim 133 \text{ mm} \times 87 \text{ mm}$)
- Heat-sealed standard pouch, stored with polycarbonate material ($\sim 150 \text{ cm}^2$ surface area)
- Uncapped glass vial (same vial as first bullet)
- Binder-clipped (semi-sealed) standard pouch ($\sim 133 \text{ mm} \times 87 \text{ mm}$)
- Capped glass vial, stored with polycarbonate
- Heat-sealed half pouch ($\sim 69 \text{ mm} \times 87 \text{ mm}$)
- Uncovered Petri dish

[00212] The packaged screening foils were stored at either 40°C (oven) or 25°C (laboratory cabinet), without relative humidity control. At pre-determined time points, three foils from each condition were washed with 5 mL of 50% v/v acetonitrile in water and analyzed on the HPLC for nicotine and m-salicylate content.

[00213] The results for the 40°C samples are presented in Figure 14 and Figure 15. Only two conditions exhibit continued loss of nicotine throughout storage duration: the open glass vial and the uncovered Petri dish. All other conditions in which the packaging was sealed demonstrated a stabilization of nicotine volatility after an initial loss.

[00214] The sealed standard sized pouches containing polycarbonate material appear to be the worst of the stabilized nicotine conditions (loss of ~ 20% nicotine content). The spray coated nicotine salt was exposed to the copolymer layer and the polycarbonate adjunct and the total volume was twice that of the half sized pouch. All other stabilized nicotine conditions lost $\leq 10\%$ of its nicotine content.

[00215] The Petri dish condition had the most rapid nicotine loss due to its storage configuration. The entire surface of the spray coated foil was continually exposed to the outside environment. Meanwhile, the foils in the open glass vials were stored upright in a narrow vial with only a small diameter of the space exposed to the outside, thereby reducing the rate of loss.

[00216] The m-salicylic acid appears to be very stable, regardless of packaging configuration. The Petri dish condition is the worst case scenario due to its maximal exposure to the outside environment. However, after four weeks of storage at 40°C with minimal humidity, the m-salicylate content remained at ~80% of initial. Otherwise, the stability results are in the range of about 100-110% of initial for all other configurations after 16 weeks of storage.

[00217] The results for the samples stored at 25°C are especially promising. Nicotine loss for all conditions up to 18 weeks of storage were within 7% of initial, except for the Petri dish condition (13% loss of nicotine content at 18 weeks). The m-salicylic acid content was stable for all eight conditions.

[00218] Loss of nicotine and m-salicylic acid due to volatility and hygroscopic effects: Nicotine salts can suffer volatility issues and can also be quite hygroscopic. For instance, nicotine sulfate absorbs water so readily that it is shipped in aqueous solution. Hygroscopic effects on nicotine m-salicylate were evaluated for 2 doses at two conditions, 22°C/44%RH (ambient condition) and 40°C/75%RH. According to the Antoine equation for water, 40°C/75%RH translates to supersaturated humidity at 22°C. Each coated EMD array was placed flat on a Petri dish (without a cover) which was then stored at either 22°C/44%RH or 40°C/75%RH. At each time point, at least 4 random individual foils were removed from the

array and each foil was extracted with 1.5 ml of 50/50 ACN/water for coated dose determination.

[00219] Overall nicotine results for the 40- $\mu\text{g}/\text{foil}$ and 170- $\mu\text{g}/\text{foil}$ conditions are summarized as follows. See Figure 14. For the 40 $\mu\text{g}/\text{foil}$ dose, coated films were relatively stable (defined as not more than 20% loss) for up to 4 hours at 60°C/35%RH, 5 days at 35°C/80%RH, and 4 weeks at 22°C/60%RH. For the 170 $\mu\text{g}/\text{foil}$ dose, coated films are stable for at least 8 hours at 60°C/35%RH, 7 days at 35°C/80%RH, 13 days at 25°C/90%RH and 4 weeks at 22°C/60%RH. Stability results demonstrate that across all stability conditions, the thicker coated films (170 $\mu\text{g}/\text{foil}$) are significantly more stable than the thinner coated films (40 $\mu\text{g}/\text{foil}$). M-salicylic acid results for 40 $\mu\text{g}/\text{foil}$ and 170 $\mu\text{g}/\text{foil}$ are summarized as follows. See Figure 15. M-salicylic acid seemed to be relatively stable for all conditions except for the 40 $\mu\text{g}/\text{foil}$ dose at 25°C/90%RH. Fortunately, this issue can be mitigated by increasing the coated film thickness.

Mechanical Stability

[00220] Fragility of the spray coating was tested using two foil arrays coated with ~200 μg of nicotine per foil (~11 μg nicotine/ mm^2 , which is about a 21 μm thick film of nicotine m-salicylate). Five foils from each array were assayed for pre-drop coated dose. Each foil array was then placed into a dose cartridge, sealed into a plastic tube, and dropped 3 times onto the floor from a height of about 1 meter. Five additional foils from each array were assayed for the post-drop coated dose. The intra-foil array coated dose was found to be 0.1 and 1.4% higher for the post-drop compared to pre-drop, with an average of ~0.8%. In these circumstances, these differences are insignificant and show that even the 200 μg nicotine equivalent coating of nicotine m-salicylate on the EMD foils are mechanically stable.

Table 3. Results of Mechanical Stability Test

Drug Film thickness (μm)*	Test condition	Nicotine coated dose (average $\pm$ 1 standard deviation)	M-salicylate coated dose (average $\pm$ 1 standard deviation)
29	Pre-drop	275 $\pm$ 3	247 $\pm$ 1
	Post-drop	277 $\pm$ 3	244 $\pm$ 3
37	Pre-drop	347 $\pm$ 6	311 $\pm$ 0
	Post-drop	335 $\pm$ 6	299 $\pm$ 7

*Assuming unit density ($1\text{g}/\text{cm}^3$)

[00221] In a follow-up study, we studied the effect of thickness on the mechanical integrity of the film. In this experiment, three foils from an array were assayed for pre-drop coated dose. Each foil array was then placed into a dose cartridge, sealed into a plastic tube, and dropped 5 times onto the floor from a height of about 1 meter. Three foils from each array were then assayed for the post-drop coated dose. The data indicate that film thicknesses corresponding to 350 μg nicotine ($\sim 37\text{ }\mu\text{m}$ thick) begin to show signs of fragility – flaking off of the drug. The drug was not lost after dropping of films of $\sim 29\text{ }\mu\text{m}$ thickness. Therefore, for mechanical purposes, nicotine m-salicylate film thicknesses should not exceed approximately 30 microns.

Example 9

Devices

[00222] Device 1: The basic design as shown in Figure 16 has been tested in the Electric Multi Dose (EMD) platform. Efficient foil packaging translates to a large number of doses. The foils are readily coated via spray process.

[00223] Device 2: See Figure 17. The doses are in the forms of small coils, wound from a solid, resistive wire such as Ni-Chrome. The coils are connected in such a way that the coil furthest from the mouthpiece offers the path of least resistance. The wire diameter is

selected such that a short current burst will heat up that coil first, and subsequently blow the fuse connection point (red dot). At that point, the coil is spent and no longer connected to the circuit. On the next heating cycle, the next coil presents the path of least resistance, so it becomes the next dose. The cycle continues until all the doses are consumed. Fail-safe design of single dose can be implemented without software. Can be a disposable unit. Form factor can be similar to a cigarette. Can leverage from wire bonding technology for coil attachment. Can be converted to software control of heating elements.

[00224] Device 3: See Figure 18. The device relies on the same fusing approach as Device 2 but it employs foils rather than coils wound from wire. A fail-safe design of single dose can be implemented without software. The device may be a disposable unit. The form factor is close to a cigarette. There is an efficient area layout which translates to higher number of doses per device. There are only two connection points. Execution of reduced area for fusing is readily accomplished with the foil. The device can easily be converted to software controlled heating elements. Flat foils will be readily coated via a spray process.

[00225] Device 4: See Figure 19. This device relies on the same fusing approach as in Devices 2 and 3. It employs foils that are wrapped in a tubular form to allow for a cigarette like form factor.

[00226] The description of the present invention has been presented for purposes of illustration and description, but is not intended to be exhaustive or limiting of the invention to the form disclosed. The scope of the present invention is limited only by the scope of the following claims. Many modifications and variations will be apparent to those of ordinary skill in the art. The embodiment described and shown in the figures was chosen and described in order to best explain the principles of the invention, the practical application, and to enable others of ordinary skill in the art to understand the invention for various embodiments with various modifications as are suited to the particular use contemplated.

CLAIMS

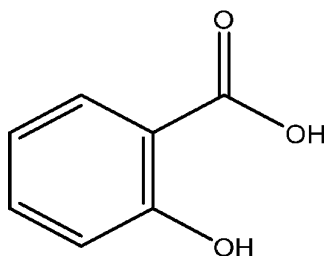
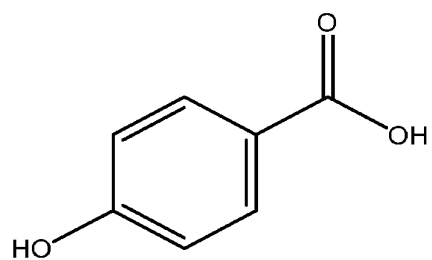
What is claimed is:

1. A nicotine salt comprising nicotine meta-salicylate salt.
2. A drug supply article comprising:
 - a heat-conductive substrate having an impermeable surface;
 - a nicotine composition comprising nicotine meta-salicylate coated on at least a portion of the surface in the form of a film having a thickness; and
 - a heat source operable to supply heat to the substrate at a rate that achieves a temperature sufficient to vaporize all or a portion of the coated nicotine composition within a period of 2 seconds;wherein the vaporized nicotine composition comprises an effective amount of the nicotine;
 - wherein the film has a thickness between 0.05 and 30 microns.
3. The drug supply article of claim 2, wherein the nicotine composition consists of nicotine meta-salicylate
4. The drug supply article of claim 2, wherein the nicotine composition comprises a pharmaceutically acceptable excipient.
5. The drug supply article of claim 2, wherein the film thickness is between 0.1 and 30 microns.
6. A pharmaceutical composition comprising nicotine meta-salicylate wherein said composition is administered through inhalation to a subject in need thereof.
7. A method of smoking cessation comprising administering an effective amount of a nicotine condensation aerosol, having an MMAD less than 3 μm and less than 5% drug degradation products, to a patient by inhalation, upon activation by the patient of the formation of, and delivery of, the condensation aerosol.
8. The method of claim 7, wherein the nicotine condensation aerosol comprises nicotine meta-salicylate.
9. A method of nicotine delivery comprising administering a nicotine condensation aerosol, having an MMAD between 0.01 and 3 μm and less than 5% drug degradation products, to a patient by inhalation, upon activation by the patient of the formation of, and delivery of, the condensation aerosol.

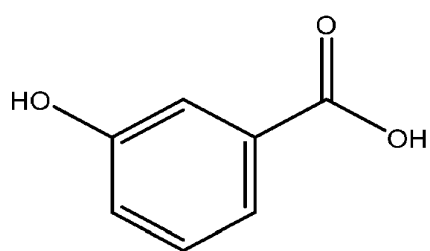
10. The method of claim 9, wherein the nicotine condensation aerosol comprises nicotine meta-salicylate.
11. A method of treating nicotine craving comprising administering a effective amount of a nicotine condensation aerosol, having an MMAD between 0.1 and 3 μm and less than 5% drug degradation products, to a patient by inhalation, upon activation by the patient of the formation of, and delivery of, the condensation aerosol.
12. The method of claim 11, wherein the nicotine condensation aerosol comprises nicotine meta-salicylate.
13. A method for effecting smoking cessation comprising administering a effective amount of a nicotine condensation aerosol, having an MMAD less than 3 μm and less than 5% drug degradation products, to a patient by inhalation, upon activation by the patient of the formation of, and delivery of, the condensation aerosol.
14. The method of claim 13, wherein the nicotine condensation aerosol comprises nicotine meta-salicylate.
15. A condensation aerosol for delivery of nicotine formed by heating a composition containing nicotine meta-salicylate coated on a solid support to produce a vapor and cooling the vapor to form a condensation aerosol comprising particles, wherein the particles comprise at least 50 percent by weight nicotine and less than 5 percent by weight nicotine degradation products, and the condensation aerosol has an MMAD between 0.2 and 5 microns.
16. The condensation aerosol according to Claim 15, wherein the condensation aerosol has an MMAD between 1 and 3 microns.
17. The condensation aerosol according to claim 15, wherein the condensation aerosol comprises 1-10% free base nicotine.
18. The condensation aerosol according to claim 15, wherein the condensation aerosol comprises 10-20% free base nicotine.
19. The condensation aerosol according to claim 15, wherein the condensation aerosol comprises 20-30% free base nicotine.
20. The condensation aerosol according to claim 15, wherein the condensation aerosol comprises 30-40% free base nicotine.
21. The condensation aerosol according to claim 15, wherein the condensation aerosol comprises 40-50% free base nicotine.

Figure 1

ortho-salicylic acid



para-salicylic acid

3-hydroxybenzoic acid
meta-salicylic acid

2/19

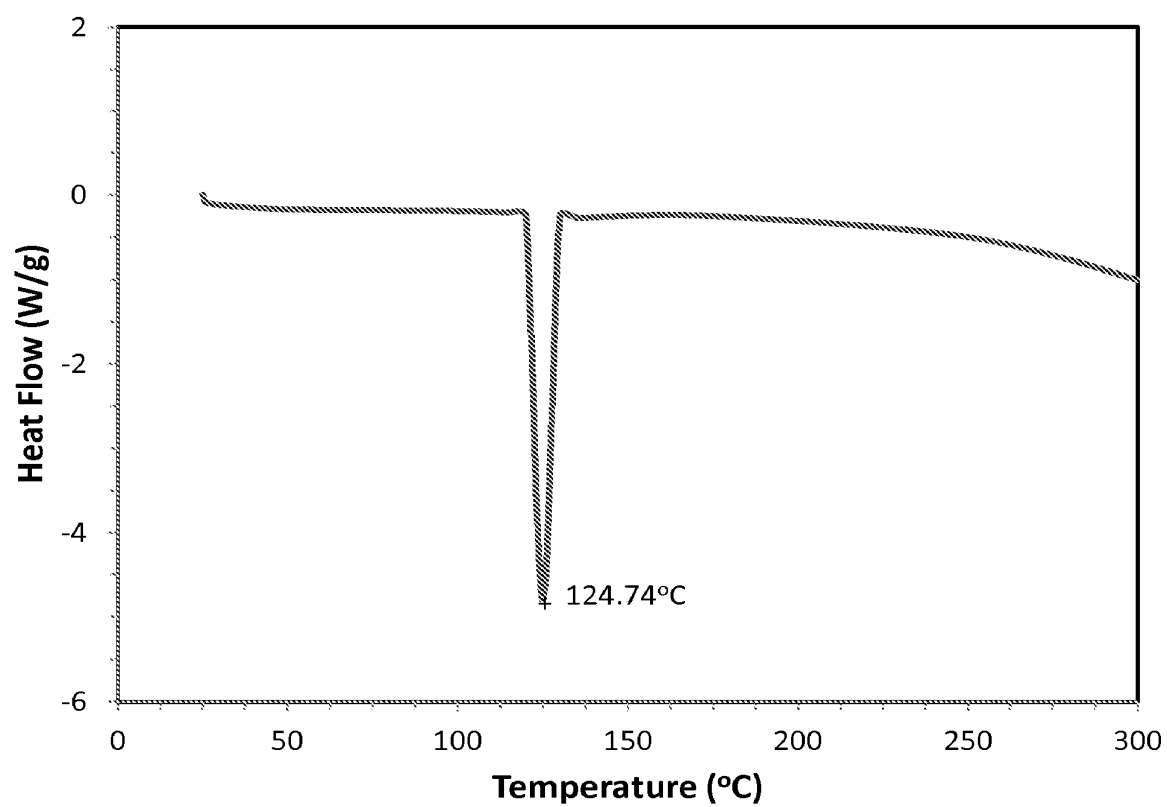
Figure 2

Figure 3

ortho isomer

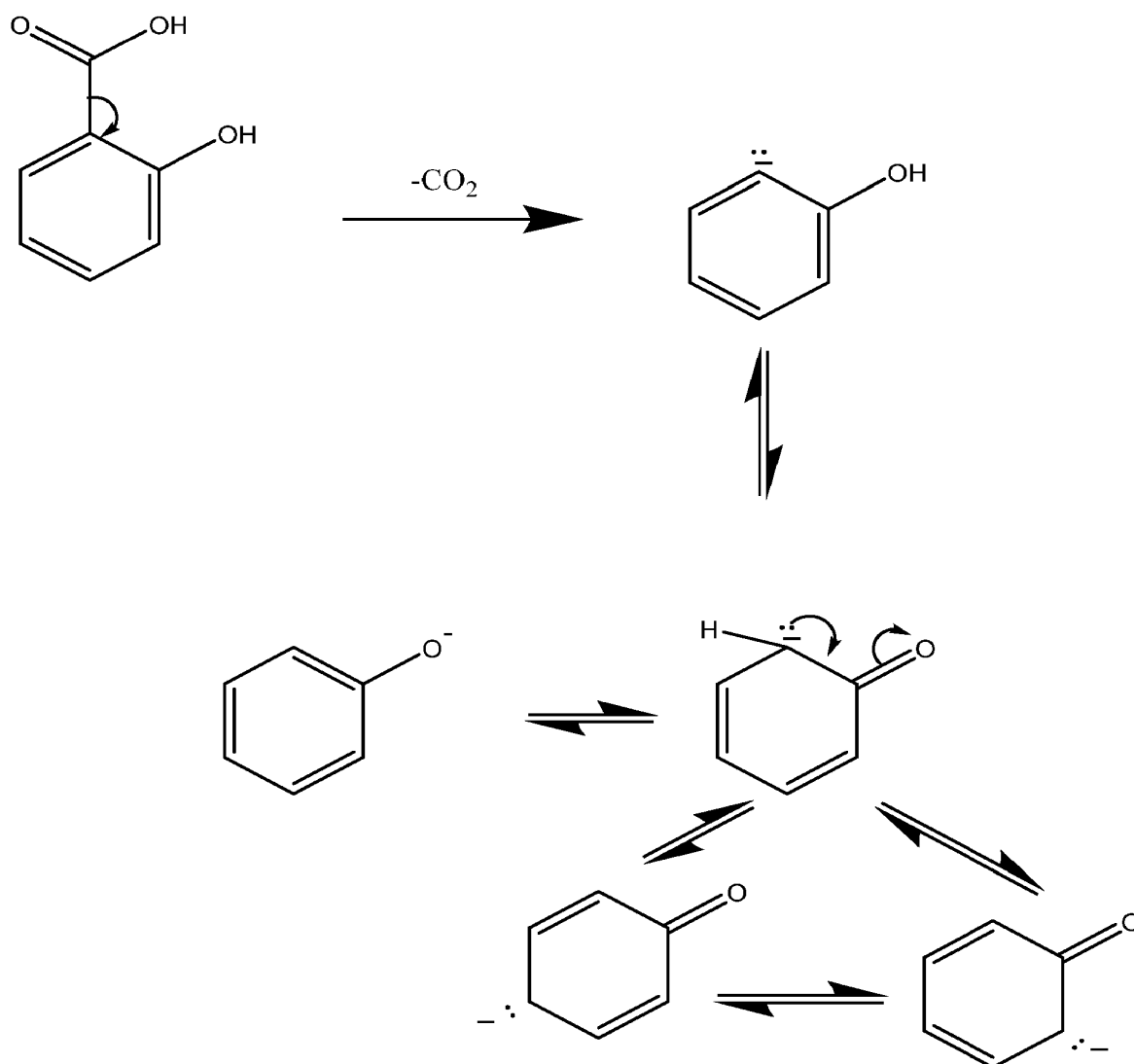
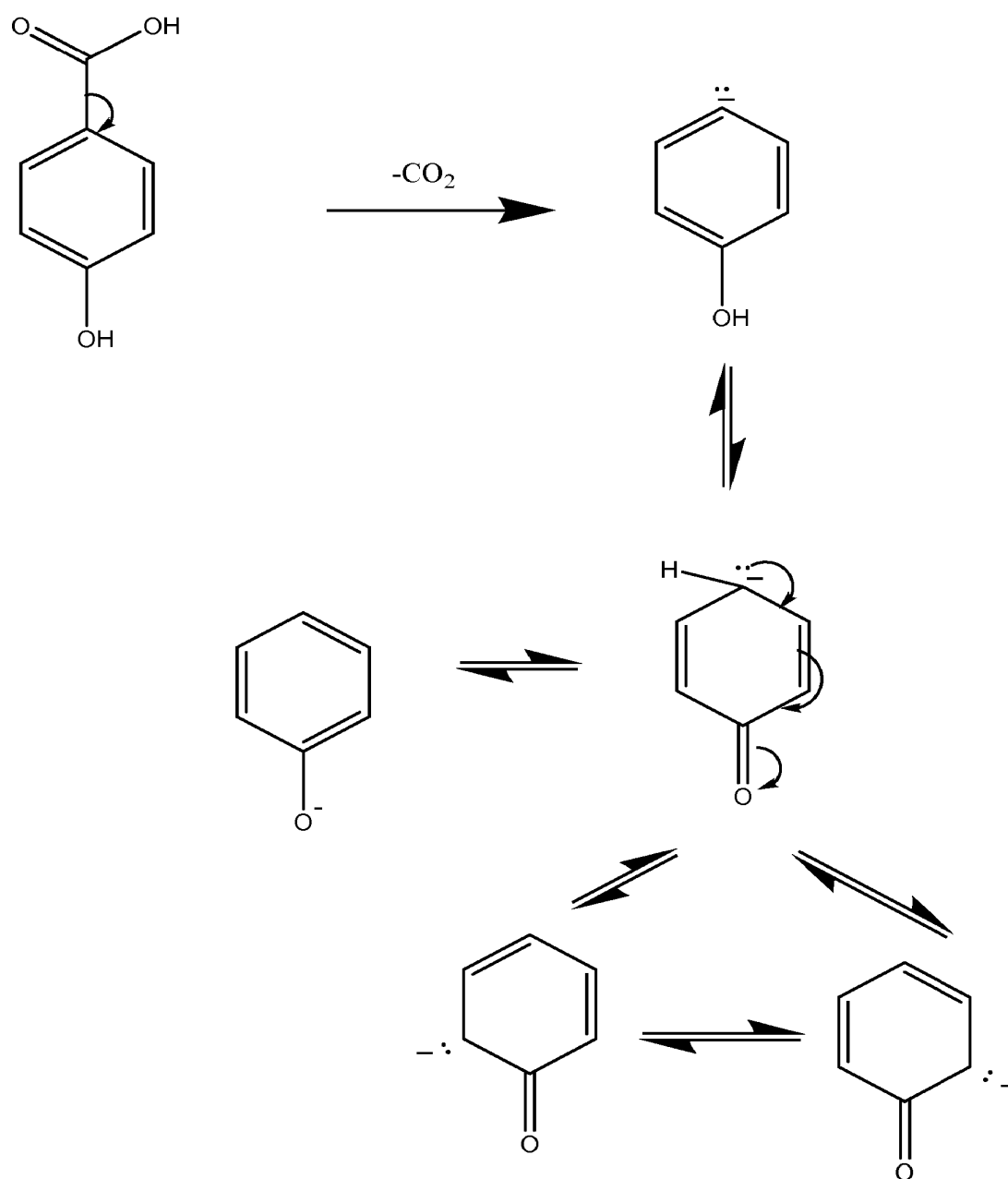


Figure 4

para isomer



5/19

Figure 5

meta isomer

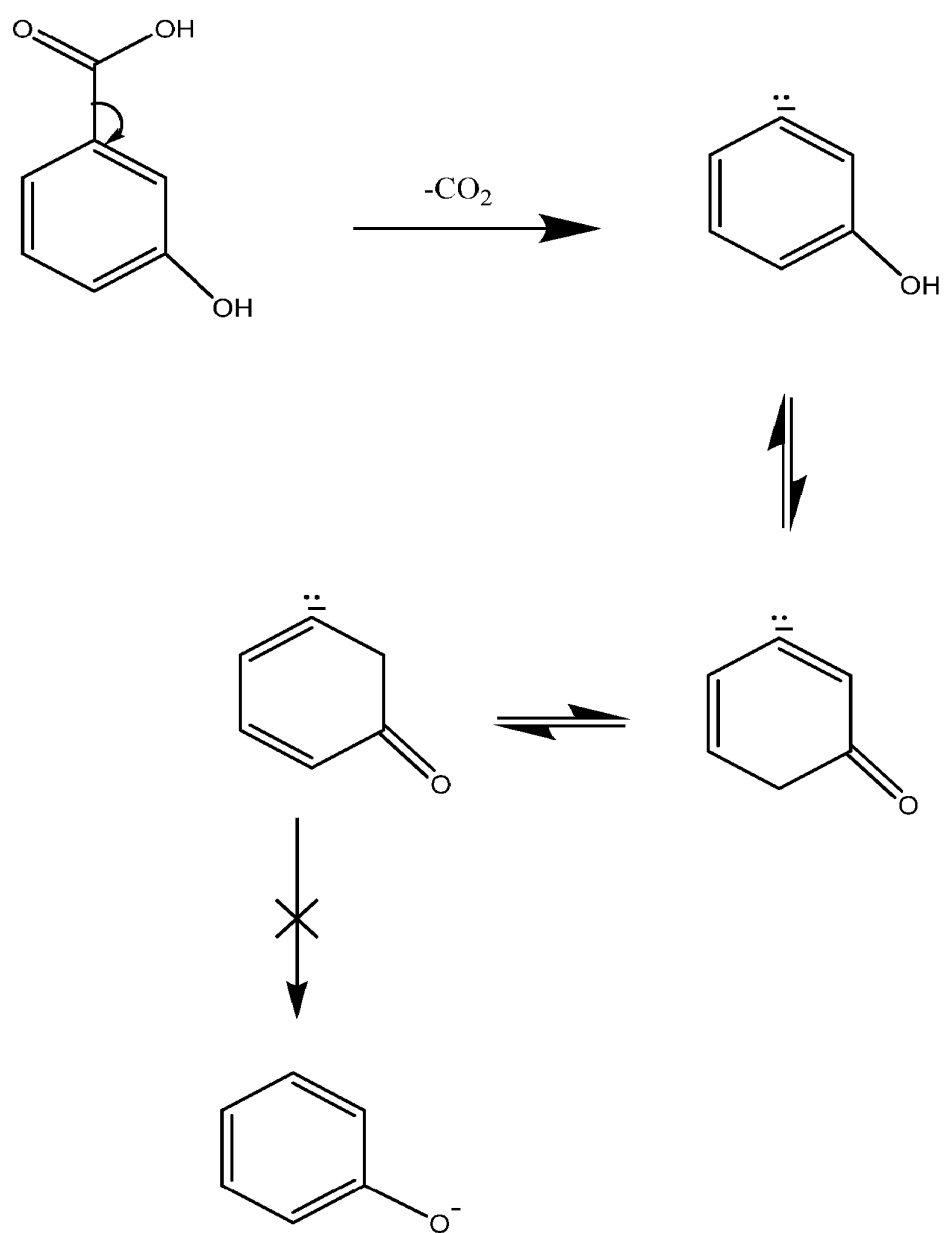
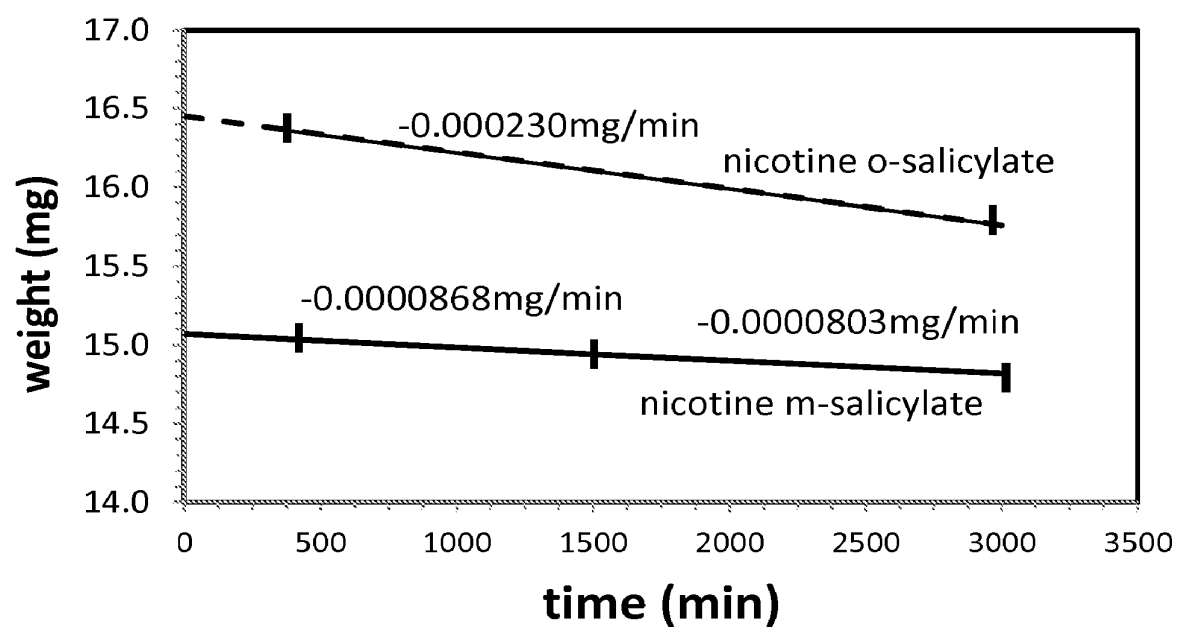


Figure 6



7/19

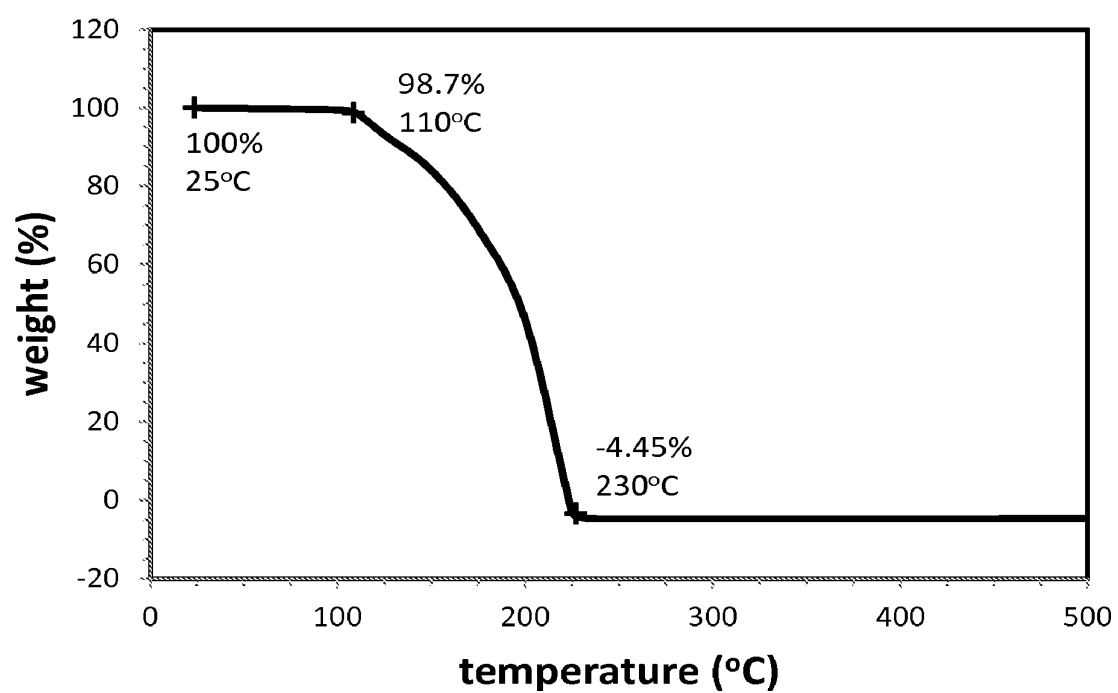
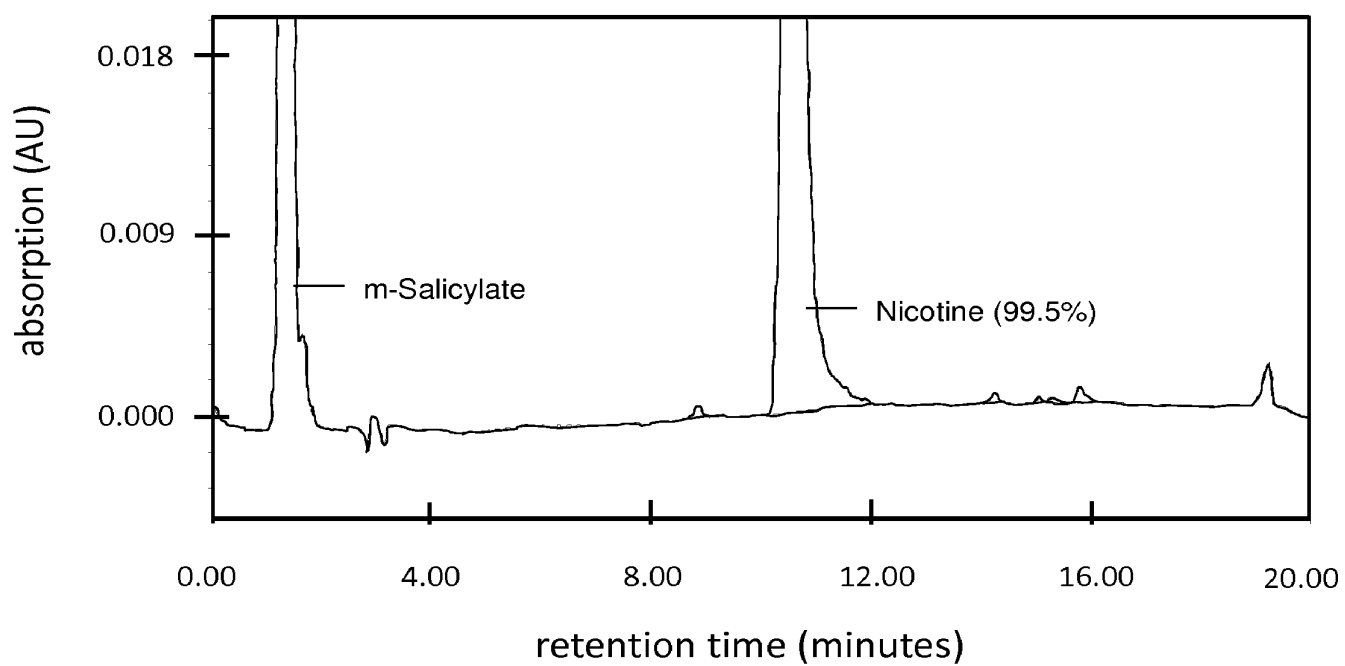
Figure 7

Figure 8

9/19

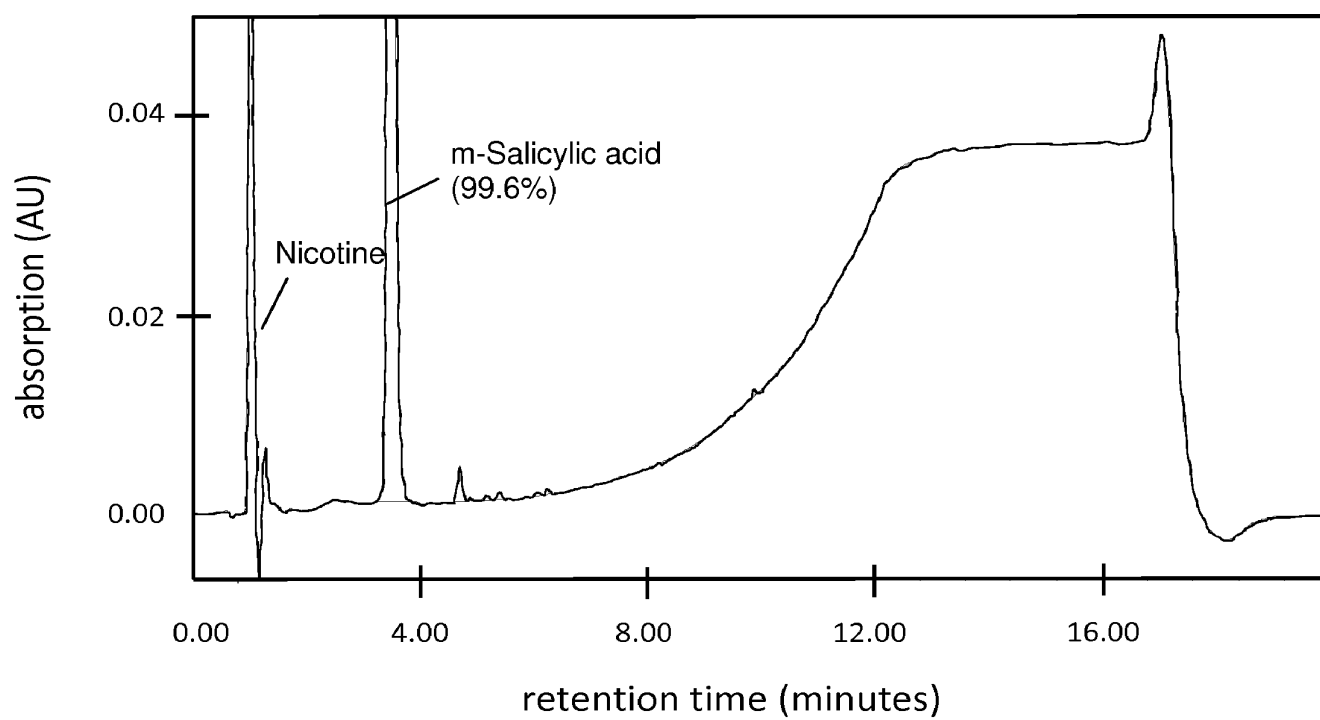
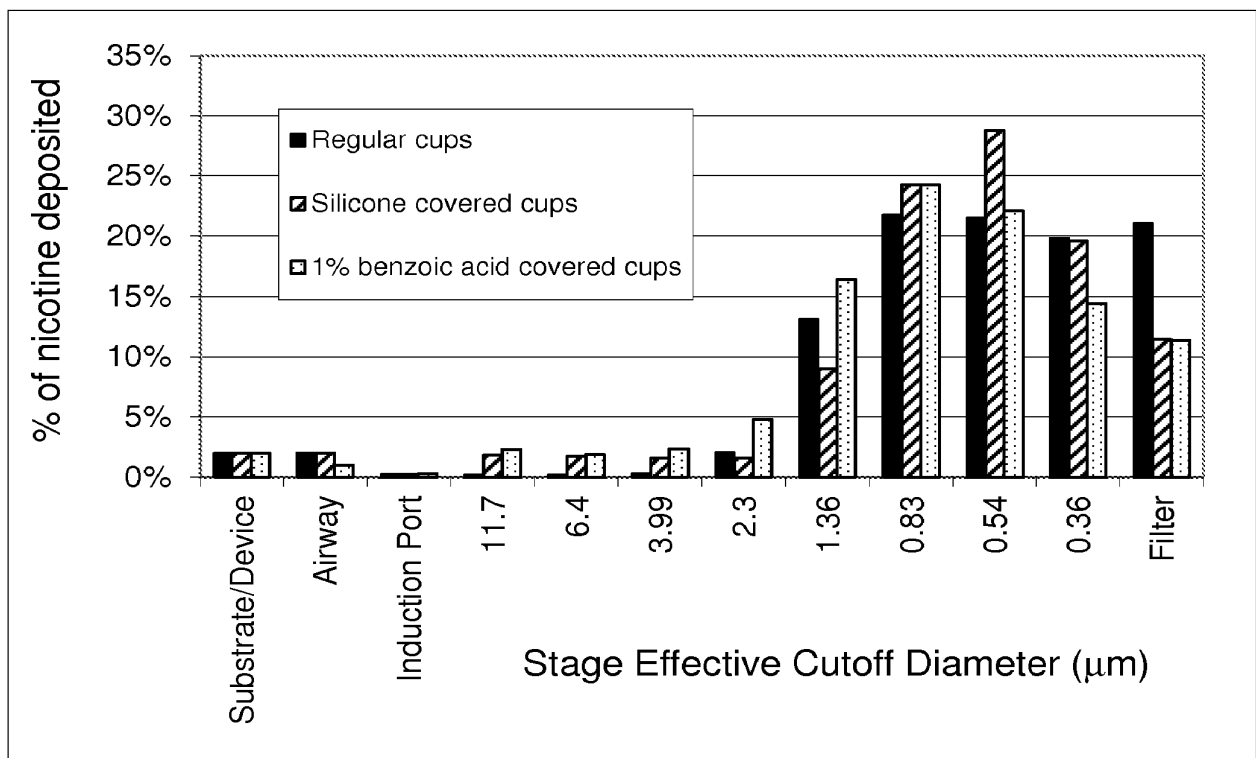
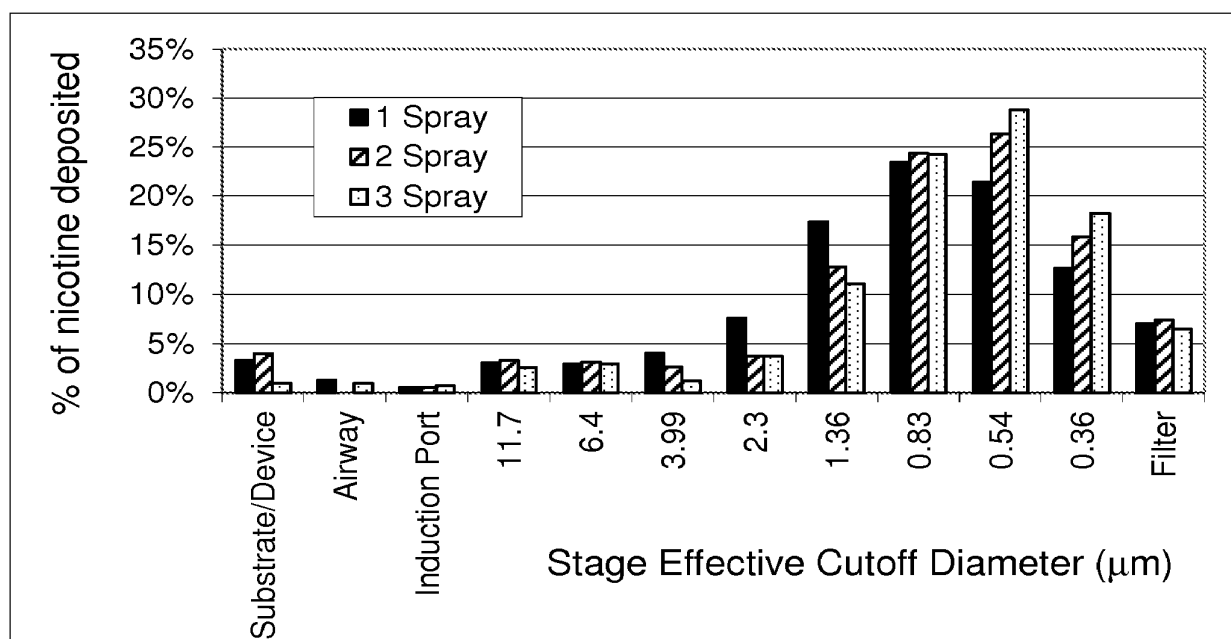
Figure 9

Figure 10



11/19

Figure 11

12/19

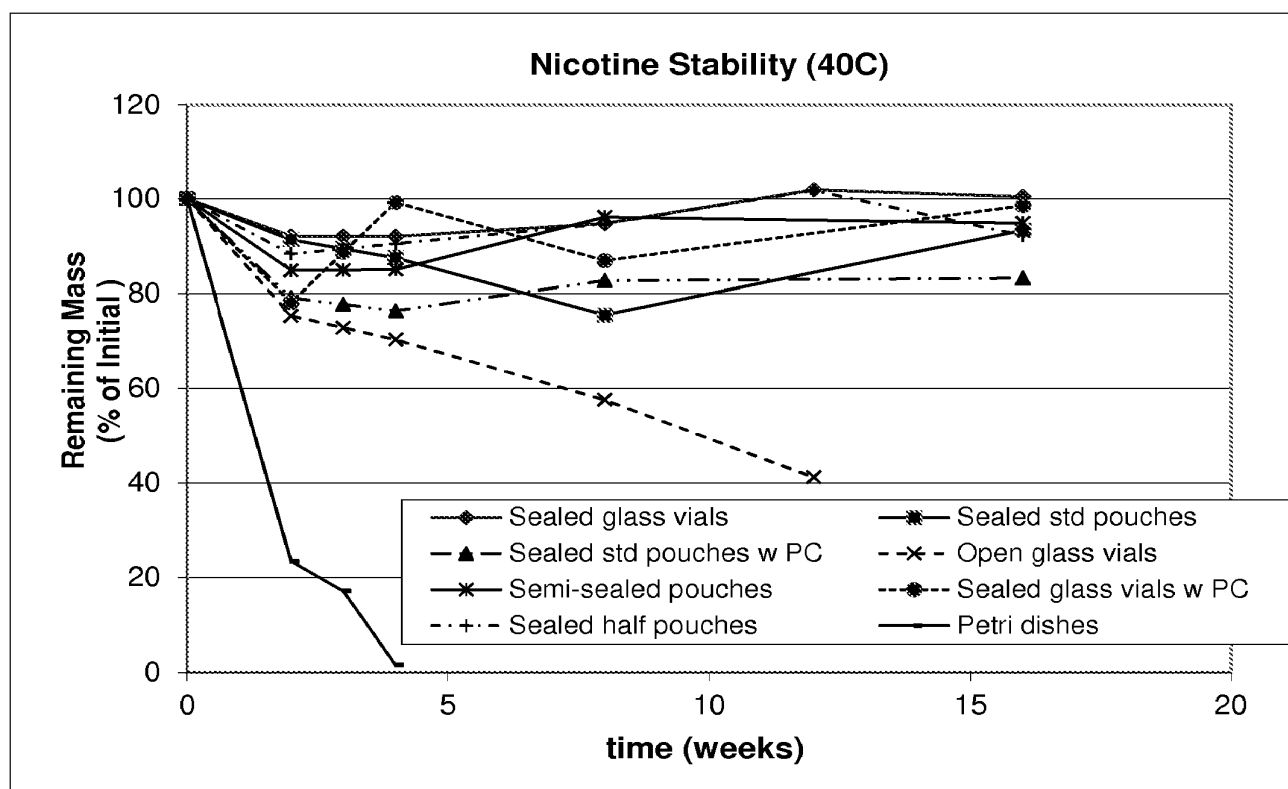
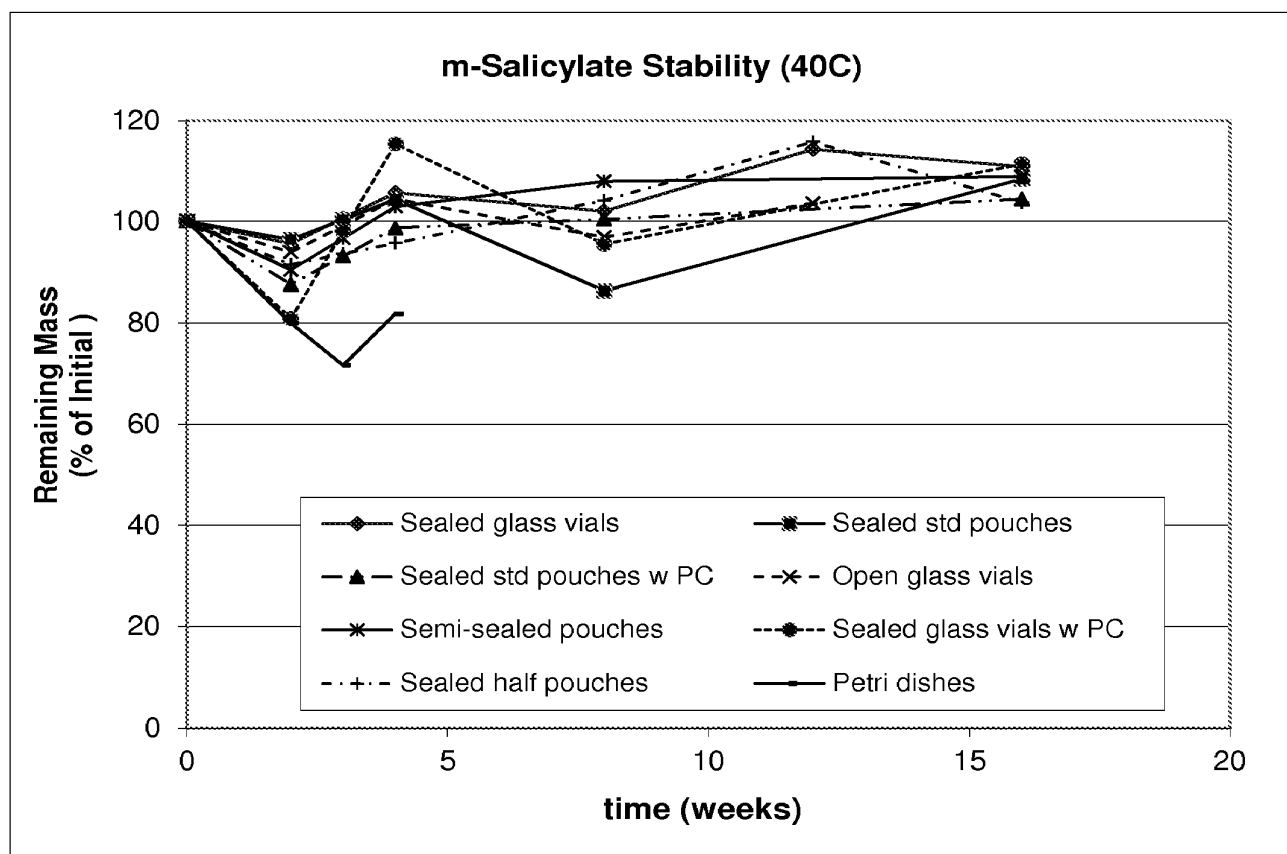
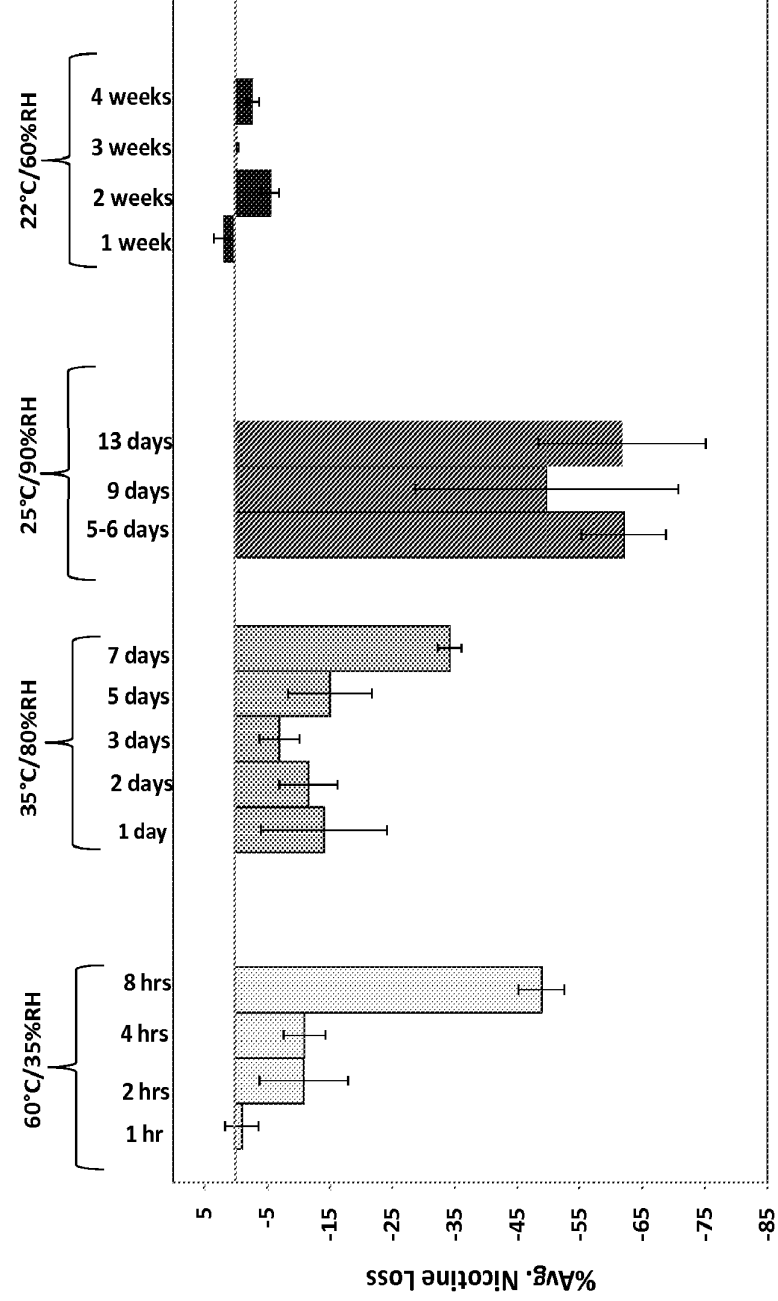
Figure 12

Figure 13



14/19

Figure 14



15/19

Figure 15

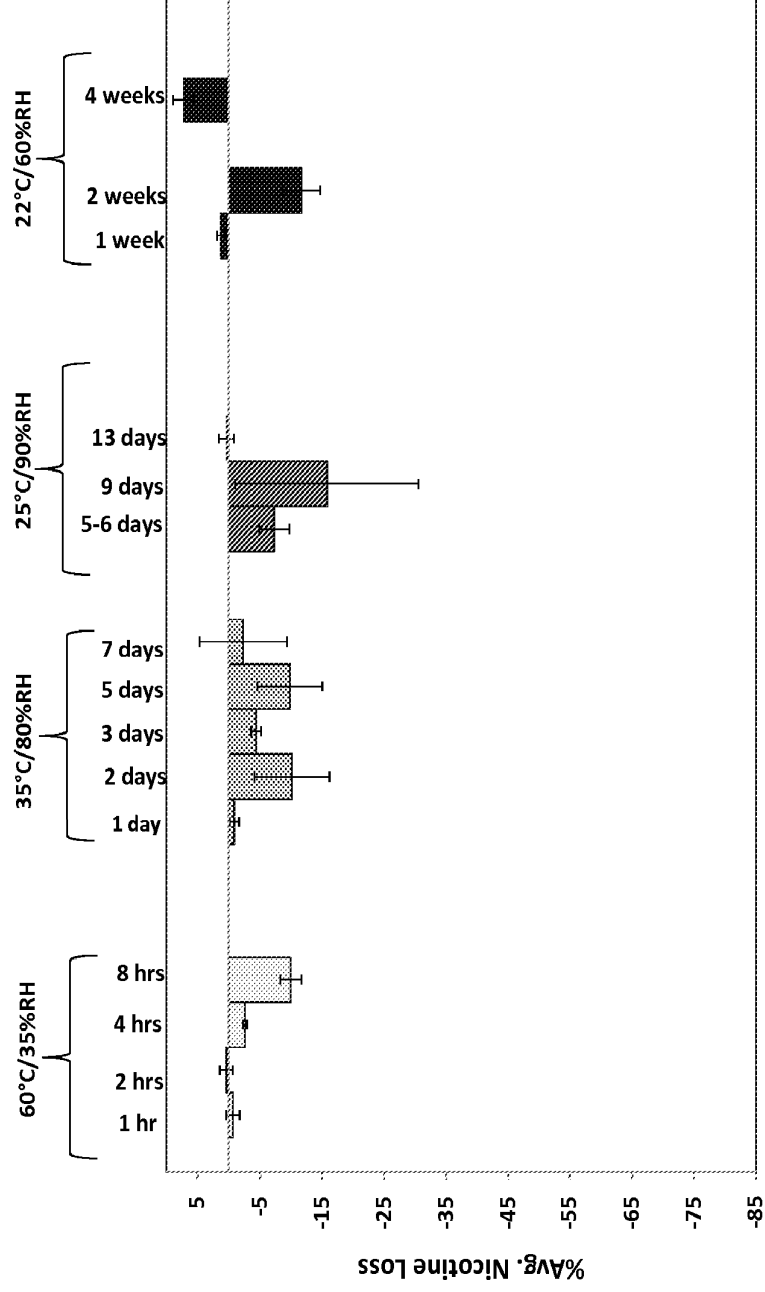


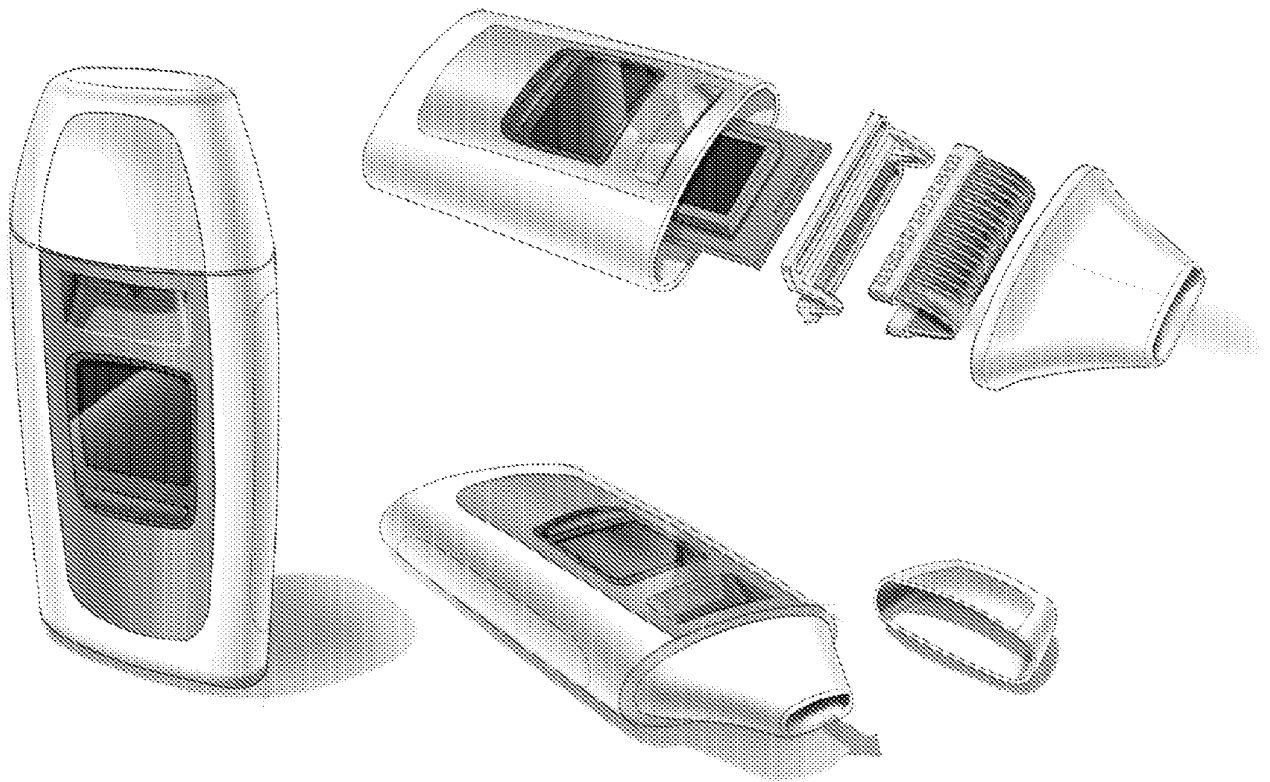
Figure 16

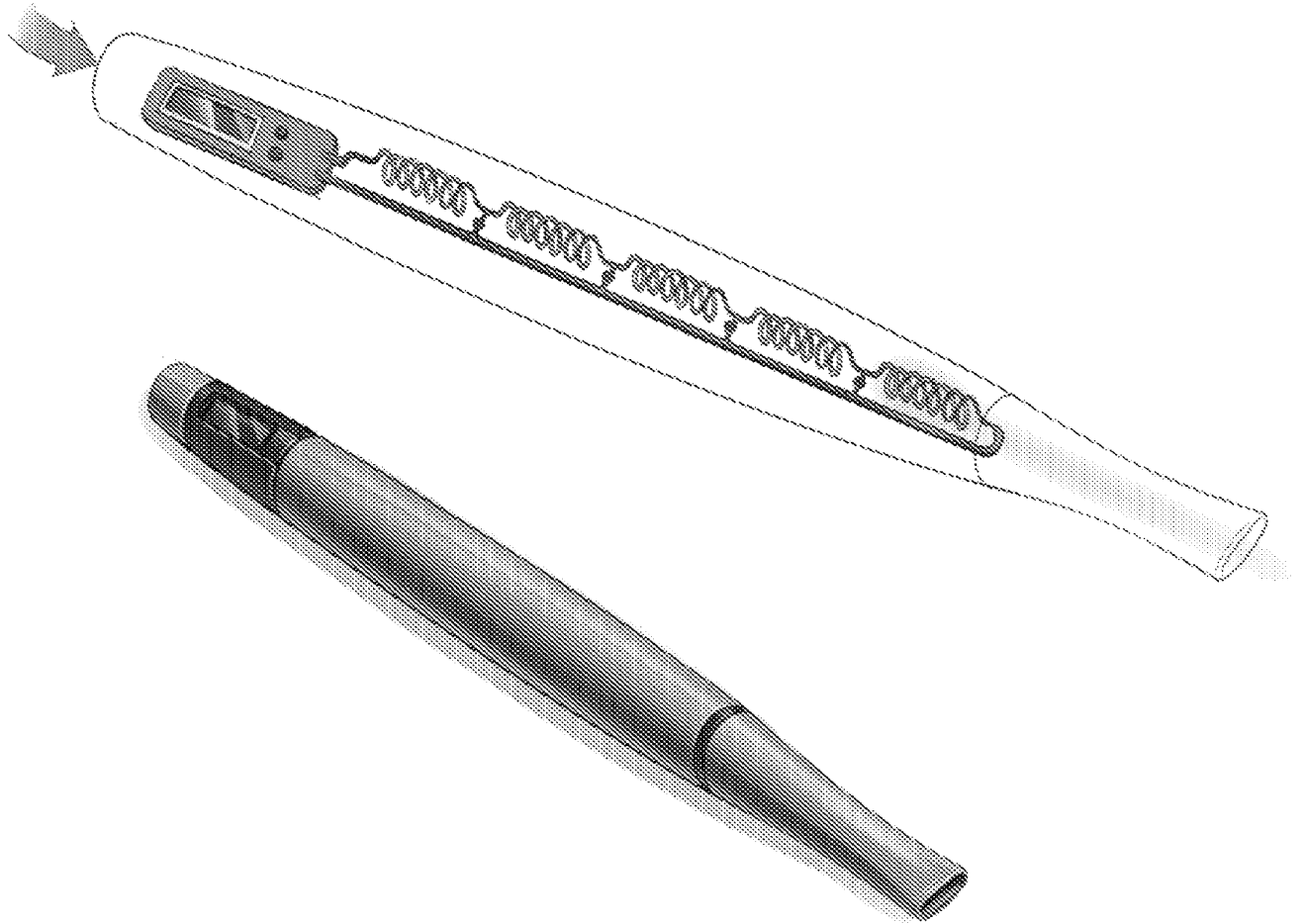
Figure 17

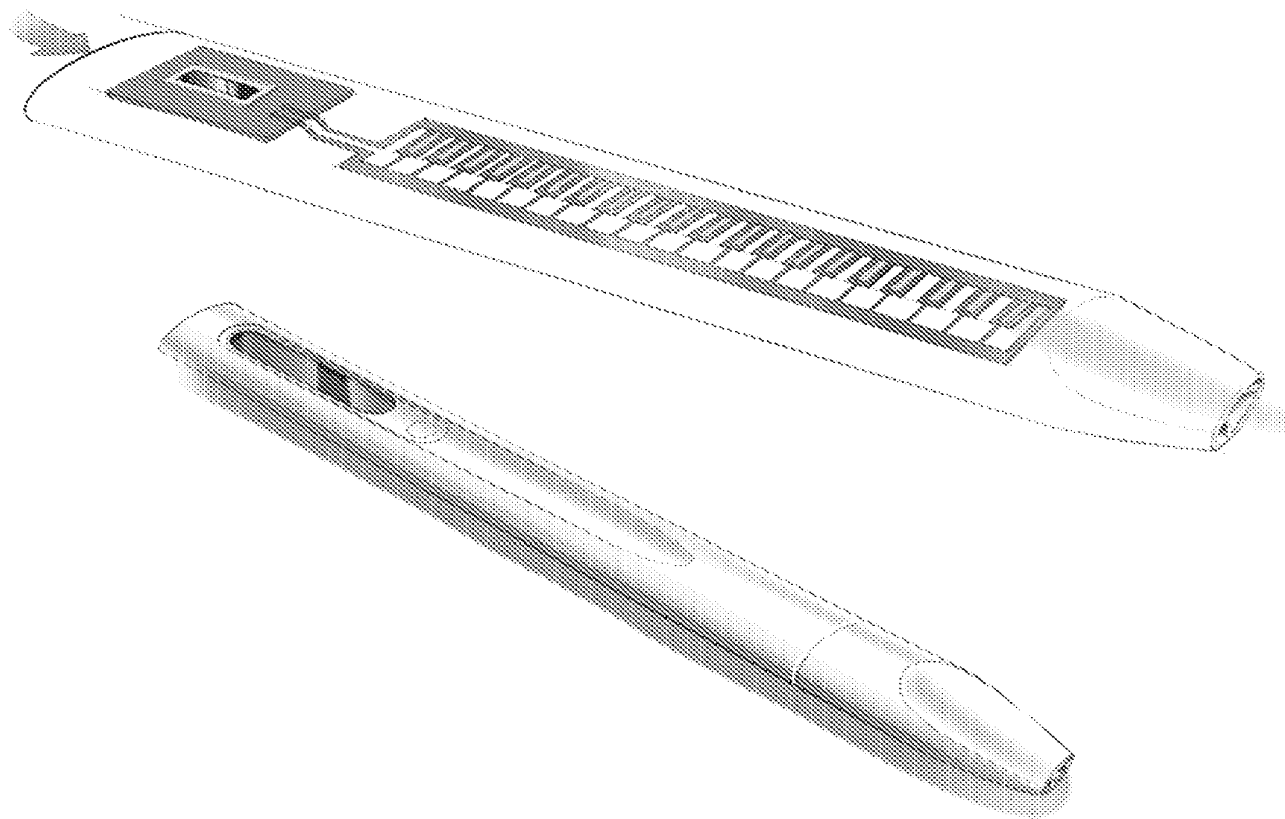
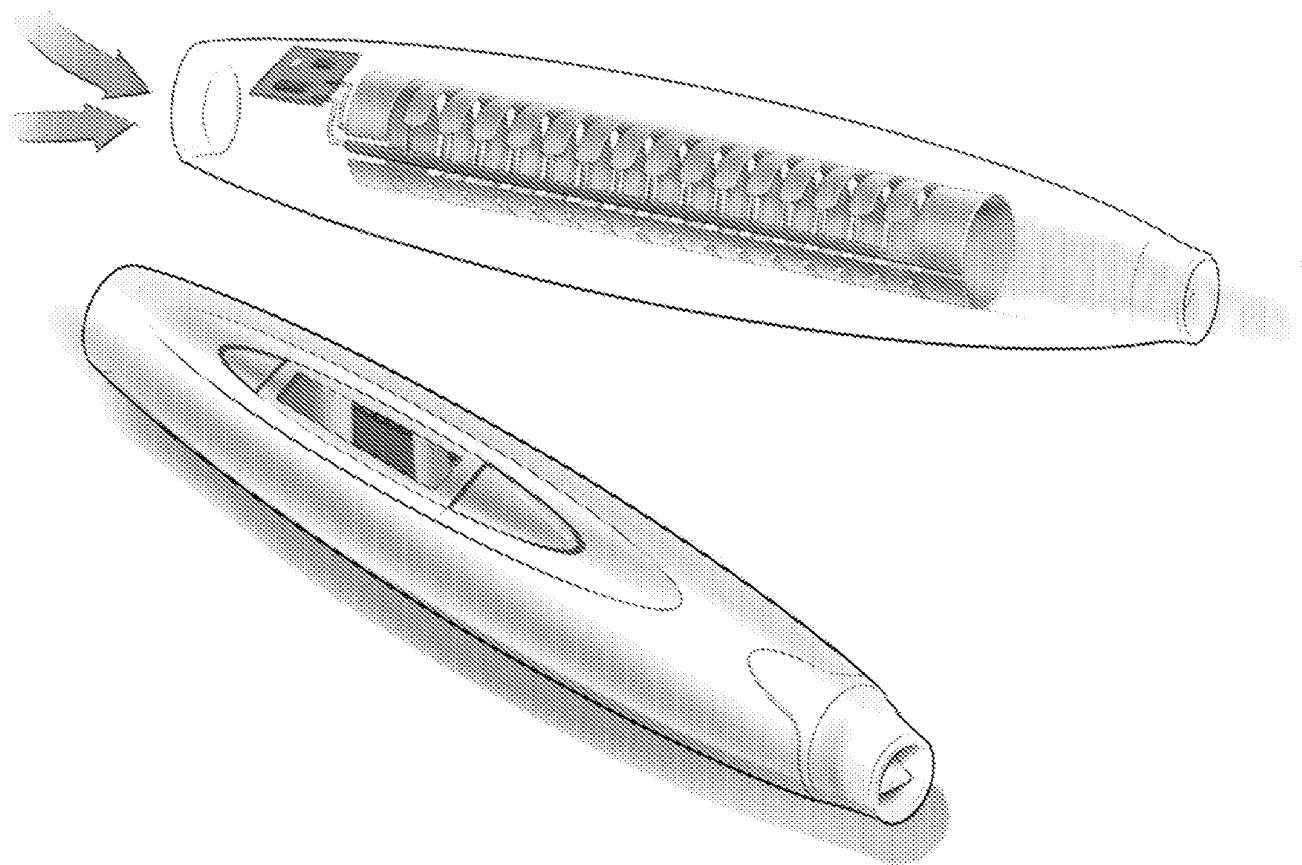
Figure 18

Figure 19

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US14/46288

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 9/00; A61M 15/06; F24J 1/00 (2014.01) CPC - A61K 9/007; A61M 11/042; Y10S 514/958 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC(8) - A61K 9/00, 31/55; A61M 11/00, 15/06; F24J 1/00; H05B 3/00 (2014.01) CPC - A61K 9/007, 31/5513; A61M 11/042, 2205/8206; F24J 1/00; Y10S 514/957, 514/958 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 128/200.23, 200.24, 202.21, 203.17 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) MicroPatent (US-G, US-A, EP-A, EP-B, WO, JP-bib, DE-C,B, DE-A, DE-T, DE-U, GB-A, FR-A); Google Scholar; PubMed; IP.com; Proquest; nicotine, meta-salicylate, 3-hydroxybenzoate, meta-hydroxybenzoate, heat-conductive substrate, delivery device, vapor*, film, thickness, pharmaceutical excipient, MMAD, mass median aerodynamic diameter, degradation, condensation aerosol, inhalation, patient, free base nicotine		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 8,235,037 B2 (HALE, RL et al.) August 7, 2012; claim 1; column 106, lines 9-24; column 9, lines 56-60; column 10, lines 56-58; column 15, lines 38-39; column 22, lines 12-36; column 25, lines 13-22; column 26, lines 4-7; column 32, lines 46-67; column 35, lines 66-67; column 36, lines 36-44	7, 9 ---
Y	US 2011/0253135 A1 (HALE, RL et al.) October 20, 2011; paragraph [0003], [0009]	11, 13
Y	US 2011/0253135 A1 (HALE, RL et al.) October 20, 2011; paragraph [0003], [0009]	11, 13
A	US 7,459,469 B2 (MUNOZ, JA et al.) December 2, 2008; column 8, lines 9-63	1, 15-21
A	US 2013/0078307 A1 (HOLTON, JR., D et al.) March 28, 2013; paragraphs [0001]-[0002], [0032]	1-6, 8, 10, 12, 14-21
A	US 7,387,788 B1 (CARRARA, RDN et al.) June 17, 2008; column 15, lines 63-67	1
A	EP 1 578 422 B1 (HANSSON, H) April 11, 2007; paragraph [0027]	1
A	US 8,003,080 B2 (RABINOWITZ, JD et al.) August 23, 2011; column 2, lines 35-61; column 3, lines 39-43; column 4 lines 3-8; column 10, lines 5-6; column 19, lines 10-11	2-6, 8, 10, 12, 14
☐ Further documents are listed in the continuation of Box C. ☐		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 12 September 2014 (12.09.2014)		Date of mailing of the international search report 02 OCT 2014
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201		Authorized officer: Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

(51) International Patent Classification:
A61K 38/22 (2006.01)(21) International Application Number:
PCT/EP2014/070034(22) International Filing Date:
19 September 2014 (19.09.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
13185245.1 19 September 2013 (19.09.2013) EP(71) Applicant: PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).(72) Inventors: ZUBER, Gérard; Route du Chalet à Gobet 2,
CH-1055 Froideville (CH). FARINE, Marie; Chemin du
Chablais 102, CH-1786 Sugiez (CH). SILVESTRINI,
Patrick Charles; Chemin de Maujobia 145, CH-2000
Neuchâtel (CH).(74) Agent: MILLBURN, Julie; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished
upon receipt of that report (Rule 48.2(g))

(54) Title: AEROSOL-GENERATING SYSTEM FOR GENERATING NICOTINE SALT PARTICLES

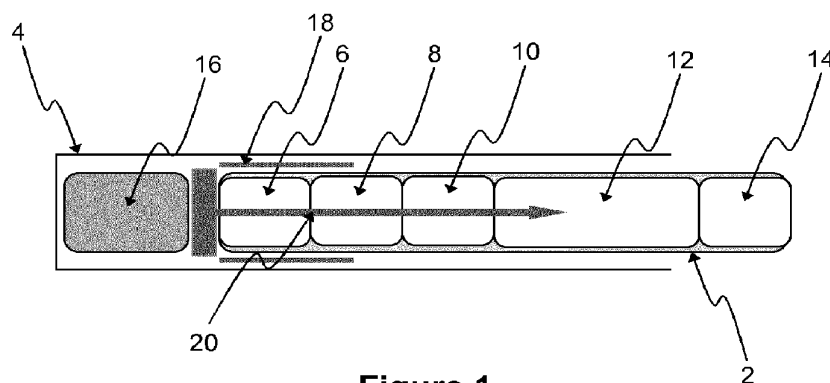


Figure 1

(57) Abstract: An aerosol-generating system comprises: a nicotine source (6); a volatile delivery enhancing compound source (10) downstream of the nicotine source, wherein the volatile delivery enhancing compound comprises an acid; heating means (18) for heating the nicotine source; and a physically separate heat transfer barrier (8) between the nicotine source and the volatile delivery enhancing compound source. The heating means is preferably configured to heat the nicotine source to a temperature of between about 80°C and about 150°C. The heat transfer barrier is preferably configured so that in use the temperature of the volatile delivery enhancing compound source is less than about 50°C when the nicotine source is heated to a temperature of between 80°C and 150°C by the heating means. The heat transfer barrier may comprise a solid material having a thermal conductivity of less than about 1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50%. Alternatively, the heat transfer barrier may comprise a cavity having a length of at least about 8mm.

AEROSOL-GENERATING SYSTEM FOR GENERATING NICOTINE SALT PARTICLES

The present invention relates to an aerosol-generating system. In particular, the present invention relates to an aerosol-generating system for generating an aerosol comprising nicotine salt particles.

Devices for delivering nicotine to a user comprising a nicotine source and a volatile delivery enhancing compound source are known. For instance, WO 2008/121610 A1 discloses a device in which nicotine and a volatile delivery enhancing compound are reacted with one another in the gas phase to form an aerosol of nicotine salt particles that is inhaled by the user. However, WO 2008/121610 A1 does not address how to optimize the ratio of nicotine and volatile delivery enhancing compound in the gas phase to minimize the amount of unreacted nicotine vapour and delivery enhancing compound vapour delivered to a user.

For example, where the vapour pressure of the volatile delivery enhancing compound is different from the vapour pressure of nicotine, this can lead to a difference in the vapour concentration of the two reactants. Differences between the vapour concentration of the volatile delivery enhancing compound and nicotine can lead to the delivery of unreacted delivery enhancing compound vapour to a user.

It is desirable to produce a maximum quantity of nicotine salt particles for delivery to a user using a minimum quantity of reactants. Consequently, it would be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 that further improves the formation of an aerosol of nicotine salt particles for delivery to a user. It is especially desirable to increase the proportion of the gas phase volatile delivery enhancing compound that is reacted with the gas phase nicotine.

According to the invention there are provided aerosol-generating systems comprising: a nicotine source; a volatile delivery enhancing compound source downstream of the nicotine source, wherein the volatile delivery enhancing compound comprises an acid; heating means configured to heat the nicotine source; and a physically separate heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source.

According to the invention there is provided an aerosol-generating system comprising: a nicotine source; a volatile delivery enhancing compound source downstream of the nicotine source, wherein the volatile delivery enhancing compound comprises an acid; heating means configured to heat the nicotine source to a temperature of between about 80°C and about 150°C; and a physically separate heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source, wherein the heat transfer barrier is configured so that in use the temperature of the volatile delivery enhancing compound source is below about 60°C when the nicotine source is heated to a temperature of between about 80°C and about 150°C by the heating means.

In certain embodiments, the heat transfer barrier comprises a solid material having a thermal conductivity of less than about 1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50%.

5 In other embodiments, the heat transfer barrier comprises a cavity having a length of at least about 8 mm.

The aerosol-generating system comprises a proximal end through which, in use, an aerosol exits the aerosol-generating system for delivery to a user. The proximal end may also be referred to as the mouth end. In use, a user draws on the proximal end of the aerosol-generating article in order to inhale an aerosol generated by the aerosol-generating system.
10 The aerosol-generating system comprises a distal end opposed to the proximal end.

As used herein, the term “longitudinal” is used to describe the direction between the proximal end and the opposed distal end of the aerosol-generating system and the term “transverse” is used to describe the direction perpendicular to the longitudinal direction.

As used herein, by “length” is meant the maximum longitudinal dimension between the
15 distal end and the proximal end of components, or portions of components, of aerosol-generating systems according to the invention.

As used herein, the terms “upstream” and “downstream” are used to describe the relative positions of components, or portions of components, of aerosol-generating systems according to the invention with respect to the direction of airflow through the aerosol-generating
20 system when a user draws on the proximal end of the aerosol-generating system.

When a user draws on the proximal end of the aerosol-generating system, air is drawn into the aerosol-generating system, passes downstream through the aerosol-generating system and exits the aerosol-generating system at the proximal end.

The proximal end of the aerosol-generating system may also be referred to as the
25 downstream end and components, or portions of components, of the aerosol-generating system may be described as being upstream or downstream of one another based on their positions relative to the airflow through the aerosol-generating system towards the proximal end.

Location of the volatile delivery enhancing compound source downstream of the nicotine source advantageously improves the consistency of the nicotine delivery of aerosol-generating
30 systems according to the invention.

Without being bound by theory, it is believed that location of the volatile delivery enhancing compound source downstream of the nicotine source in aerosol-generating systems according to the invention reduces or prevents deposition of volatile delivery enhancing compound vapour released from the volatile delivery enhancing compound source on the
35 nicotine source during use. This reduces fading over time of the nicotine delivery in aerosol-generating systems according to the invention.

The heat transfer barrier separates the nicotine source and the volatile delivery enhancing compound source. The heat transfer barrier is configured to reduce heat transfer between the nicotine source and the volatile delivery enhancing compound source.

Inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source advantageously enables the volatile delivery enhancing compound source of aerosol-generating systems according to the invention to be maintained at a lower temperature while the nicotine source is heated to a higher temperature by the heating means. In particular, inclusion of a heat transfer barrier advantageously enables the nicotine delivery of aerosol-generating systems according to the invention to be significantly increased by increasing the temperature of the nicotine source while the volatile delivery enhancing compound source is maintained at a temperature below the thermal decomposition temperature of the volatile delivery enhancing compound.

As used herein, "heat transfer barrier" is used to describe a physical barrier that reduces the amount of heat transferred from the nicotine source to the volatile delivery enhancing compound source compared to an aerosol-generating system in which no barrier is present. The physical barrier may comprise a solid material. Alternatively or in addition, the physical barrier may comprise a gas, vacuum or partial vacuum between the nicotine source and the volatile delivery enhancing compound source.

The heat transfer barrier is physically separate from the nicotine source and the volatile delivery enhancing compound source. As used herein, by "physically separate" it is meant the heat transfer barrier does not form part of the nicotine source or the volatile delivery enhancing compound source. That is, aerosol-generating systems according to the invention comprise a heat transfer barrier in addition to a nicotine source and a volatile delivery enhancing compound source.

Preferably, the heating means is configured to heat the nicotine source to a temperature of between about 80°C and about 150°C. More preferably, the heating means is configured to heat the nicotine source to a temperature of between about 100°C and about 120°C. In certain embodiments, the heating means is configured to heat the nicotine source to a temperature of about 110°C.

The heating means may comprise any heater capable of heating the nicotine source to a temperature of between about 80°C and about 150°C.

Differential heating of the nicotine source and the volatile delivery enhancing compound source advantageously enables the vapour concentrations of the nicotine and the volatile delivery enhancing compound to be controlled and balanced proportionally to yield an efficient reaction stoichiometry. This advantageously improves the efficiency of the formation of an aerosol and the consistency of nicotine delivery to a user.

In combination, location of the volatile delivery enhancing compound source downstream of the nicotine source and inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source thereby advantageously reduces variability in the nicotine delivery of aerosol-generating systems according to the invention. In particular, in combination, location of the volatile delivery enhancing compound source downstream of the nicotine source and inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source advantageously enables the molar ratio of nicotine vapour to volatile delivery enhancing compound vapour to be kept substantially constant during use of aerosol-generating systems according to the invention.

By enabling the molar ratio of nicotine vapour to volatile delivery enhancing compound vapour to be kept substantially constant during use, location of the volatile delivery enhancing compound source downstream of the nicotine source and inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source also advantageously enables delivery of unreacted delivery enhancing compound vapour to a user to be reduced without inclusion of a specialised filter or other volatile delivery enhancing compound removal means downstream of the volatile delivery enhancing compound source.

The constructions, dimensions and physical properties of the heat transfer barrier may be selected to achieve a sufficient reduction in heat transfer between the nicotine source and the volatile delivery enhancing compound source to maintain the volatile delivery enhancing compound source below a desired temperature.

Preferably, the heat transfer barrier is configured so that in use the volatile delivery enhancing compound source is maintained at a temperature of less than about 60°C. More preferably, the heat transfer barrier is configured so that in use the volatile delivery enhancing compound source is maintained at a temperature of less than about 50°C. In certain embodiments, the heating means is configured so that in use the volatile delivery enhancing compound source is maintained at a temperature of less than or equal to about 45°C.

The heat transfer barrier may be formed from a thermally insulating material.

In certain embodiments, the heat transfer barrier comprises a solid material having a thermal conductivity of less than about 1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50%. Preferably the heat transfer element comprises a solid material having a thermal conductivity of less than about 5W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50% as measured using the modified transient plane source (MTPS) method. More preferably, the heat transfer element comprises a solid material having a thermal conductivity of less than about 1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50% as measured using the modified transient plane source (MTPS) method. In certain embodiments, the heat transfer element comprises a solid material having a thermal conductivity of less than

about 0.1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50% as measured using the modified transient plane source (MTPS) method.

The heat transfer barrier may comprise any suitable thermally insulating material. Preferably the thermally insulating material is a food-safe material. Suitable thermally insulating materials include, but are not limited to, plastic materials, such as polyurethane, polyethylene (PE), polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), glass, paper, cardboard and cellulose fibre. Those skilled in the art will be aware of other suitable thermally insulating materials.

In other embodiments, the heat transfer barrier may comprise a cavity.

As used herein with reference to the heat transfer barrier, the term “cavity” is used to describe a gas-filled space or compartment or a space or compartment comprising a region of reduced air pressure, such as a vacuum or partial vacuum. Preferably, the cavity is a gas-filled space. More preferably, the cavity is an air-filled space.

In such embodiments, preferably the heat transfer barrier comprises a cavity having a length of at least about 8 mm. More preferably, the heat transfer barrier comprises a cavity having a length of at least about 9 mm. In certain embodiments, the heat transfer barrier comprises a cavity having a length of at least about 10 mm.

Aerosol-generating systems according to the invention comprise a volatile delivery enhancing compound source. The volatile delivery enhancing compound comprises an acid. As used herein, by “volatile” it is meant the delivery enhancing compound has a vapour pressure of at least about 20 Pa. Unless otherwise stated, all vapour pressures referred to herein are vapour pressures at 25°C measured in accordance with ASTM E1194 – 07.

Preferably, the volatile delivery enhancing compound has a vapour pressure of at least about 50 Pa, more preferably at least about 75 Pa, most preferably at least 100 Pa at 25°C.

Preferably, the volatile delivery enhancing compound has a vapour pressure of less than or equal to about 400 Pa, more preferably less than or equal to about 300 Pa, even more preferably less than or equal to about 275 Pa, most preferably less than or equal to about 250 Pa at 25°C.

In certain embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 20 Pa and about 400 Pa, more preferably between about 20 Pa and about 300 Pa, even more preferably between about 20 Pa and about 275 Pa, most preferably between about 20 Pa and about 250 Pa at 25°C.

In other embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 50 Pa and about 400 Pa, more preferably between about 50 Pa and about 300 Pa, even more preferably between about 50 Pa and about 275 Pa, most preferably between about 50 Pa and about 250 Pa at 25°C.

In further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 75 Pa and about 400 Pa, more preferably between about 75 Pa and about 300 Pa, even more preferably between about 75 Pa and about 275 Pa, most preferably between about 75 Pa and about 250 Pa at 25°C.

5 In yet further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 100 Pa and about 400 Pa, more preferably between about 100 Pa and about 300 Pa, even more preferably between about 100 Pa and about 275 Pa, most preferably between about 100 Pa and about 250 Pa at 25°C.

The volatile delivery enhancing compound may comprise a single compound.
10 Alternatively, the volatile delivery enhancing compound may comprise two or more different compounds.

Where the volatile delivery enhancing compound comprises two or more different compounds, the two or more different compounds in combination have a vapour pressure of at least about 20 Pa at 25°C.

15 Preferably, the volatile delivery enhancing compound is a volatile liquid.

The volatile delivery enhancing compound may comprise a mixture of two or more different liquid compounds.

The volatile delivery enhancing compound may comprise an aqueous solution of one or more compounds. Alternatively the volatile delivery enhancing compound may comprise a non-
20 aqueous solution of one or more compounds.

The volatile delivery enhancing compound may comprise two or more different volatile compounds. For example, the volatile delivery enhancing compound may comprise a mixture of two or more different volatile liquid compounds.

Alternatively, the volatile delivery enhancing compound may comprise one or more non-
25 volatile compounds and one or more volatile compounds. For example, the volatile delivery enhancing compound may comprise a solution of one or more non-volatile compounds in a volatile solvent or a mixture of one or more non-volatile liquid compounds and one or more volatile liquid compounds.

The volatile delivery enhancing compound comprises an acid. The volatile delivery
30 enhancing compound may comprise an organic acid or an inorganic acid. Preferably, the volatile delivery enhancing compound comprises an organic acid, more preferably a carboxylic acid. In certain particularly preferred embodiments, the volatile delivery enhancing compound comprises a 2-oxo acid. In other particularly preferred embodiments, the volatile delivery enhancing compound comprises an alpha hydroxy acid.

35 Examples of suitable carboxylic acids include those selected from the group consisting of 3-methyl-2-oxopentanoic acid, pyruvic acid, 2-oxopentanoic acid, 4-methyl-2-oxopentanoic acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid, lactic acid and combinations thereof. In

particularly preferred embodiments, the volatile delivery enhancing compound comprises pyruvic acid or lactic acid.

In preferred embodiments, the volatile delivery enhancing compound source comprises a sorption element and a volatile delivery enhancing compound sorbed on the sorption element.

5 As used herein, by "sorbed" it is meant that the volatile delivery enhancing compound is adsorbed on the surface of the sorption element, or absorbed in the sorption element, or both adsorbed on and absorbed in the sorption element. Preferably, the volatile delivery enhancing compound is adsorbed on the sorption element.

10 The sorption element may be formed from any suitable material or combination of materials. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and combinations thereof. For example, the sorption element may comprise both PE and PET.

15 In preferred embodiments, the sorption element is a porous sorption element.

For example, the sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

20 The sorption element is preferably chemically inert with respect to the volatile delivery enhancing compound.

The sorption element may have any suitable size and shape.

In certain preferred embodiments, the sorption element is a substantially cylindrical plug. In certain particularly preferred embodiments, the sorption element is a porous substantially cylindrical plug.

25 In other preferred embodiments, the sorption element is a substantially cylindrical hollow tube. In other particularly preferred embodiments, the sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the sorption element may be chosen to allow a desired amount of volatile delivery enhancing compound to be sorbed on the sorption element.

30 The volatile delivery enhancing compound source should comprise sufficient volatile delivery enhancing compound to generate a desired quantity of aerosol for delivery to a user.

The sorption element advantageously acts as a reservoir for the volatile delivery enhancing compound.

Aerosol-generating systems according to the invention also comprise a nicotine source.

35 Nicotine has a vapour pressure of between about 5 Pa and about 6 Pa at 25°C.

The nicotine source may comprise one or more of nicotine, nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate, or a nicotine derivative.

The nicotine source may comprise natural nicotine or synthetic nicotine.

The nicotine source may comprise pure nicotine, a solution of nicotine in an aqueous or non-aqueous solvent or a liquid tobacco extract.

5 The nicotine source may further comprise an electrolyte forming compound. The electrolyte forming compound may be selected from the group consisting of alkali metal hydroxides, alkali metal oxides, alkali metal salts, alkaline earth metal oxides, alkaline earth metal hydroxides and combinations thereof.

10 For example, the nicotine source may comprise an electrolyte forming compound selected from the group consisting of potassium hydroxide, sodium hydroxide, lithium oxide, barium oxide, potassium chloride, sodium chloride, sodium carbonate, sodium citrate, ammonium sulfate and combinations thereof.

In certain embodiments, the nicotine source may comprise an aqueous solution of nicotine, nicotine base, a nicotine salt or a nicotine derivative and an electrolyte forming compound.

15 Alternatively or in addition, the nicotine source may further comprise other components including, but not limited to, natural flavours, artificial flavours and antioxidants.

The nicotine source may comprise a sorption element and nicotine sorbed on the sorption element.

20 As used herein, by "sorbed" it is meant that the nicotine is adsorbed on the surface of the sorption element, or absorbed in the sorption element, or both adsorbed on and absorbed in the sorption element.

The sorption element may be formed from any suitable material or combination of materials. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET),
25 polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and mixtures thereof. For instance, the sorption element may comprise a mixture of PE and PET.

In preferred embodiments, the sorption element is a porous sorption element.

30 For example, the sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

The sorption element is preferably chemically inert with respect to the nicotine.

The sorption element may have any suitable size and shape.

In certain preferred embodiments, the sorption element is a substantially cylindrical plug.

35 In certain particularly preferred embodiments, the sorption element is a porous substantially cylindrical plug.

In other preferred embodiments, the sorption element is a substantially cylindrical hollow tube. In other particularly preferred embodiments, the sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the sorption element may be chosen to allow a desired amount of nicotine to be sorbed on the sorption element. Those skilled in the art will be able to design a suitable sorption element according to the desired function thereof.

The nicotine source should comprise sufficient nicotine to generate a desired quantity of aerosol for delivery to a user.

The sorption element advantageously acts as a reservoir for the nicotine.

It will be appreciated that the nicotine source and the delivery enhancing compound source may comprise sorption elements having the same or different composition.

It will be appreciated that the nicotine source and the delivery enhancing compound source may comprise sorption elements of the same or different size and shape.

Aerosol-generating systems according to the invention may comprise a first compartment comprising the nicotine source and a second compartment comprising the volatile delivery enhancing compound source.

In such embodiments, the aerosol-generating system may further comprise a third compartment downstream of the second compartment.

Alternatively or in addition, in such embodiments, the aerosol-generating system may further comprise a mouthpiece downstream of the second compartment and the third compartment, where included.

In certain preferred embodiments, aerosol-generating systems according to the invention may comprise a housing comprising an air inlet and an air outlet, the housing comprising in series from air inlet to air outlet: a first compartment comprising the nicotine source in communication with the air inlet; a second compartment comprising the volatile delivery enhancing compound source in communication with the first compartment; and a heat transfer barrier between the first compartment and the second compartment, wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

As used herein, the term "air inlet" is used to describe one or more apertures through which air may be drawn into the housing.

As used herein, the term "air outlet" is used to describe one or more apertures through which air may be drawn out of the housing.

The air outlet is located at the proximal end of the housing of the aerosol-generating system. The air inlet may be located at the distal end of the housing of the aerosol-generating system. Alternatively, the air inlet may be located between the proximal end and the distal end of the housing of the aerosol-generating system.

As used herein, by "series" it is meant that the first compartment and the second compartment are arranged within the housing so that in use air passing into the housing through the air inlet, through the housing and out of the housing through the air outlet first passes the first compartment and then passes the second compartment. That is, the first compartment is downstream of the air inlet, the second compartment is downstream of the first compartment and the air outlet is downstream of the second compartment.

Nicotine vapour is released from the nicotine source in the first compartment into the air as it passes downstream through the housing from the air inlet towards the air outlet. Volatile delivery enhancing compound vapour is also released from the volatile delivery enhancing compound source in the second compartment into the air as it passes further downstream through the housing from the first compartment towards the air outlet. The nicotine vapour reacts with the volatile delivery enhancing compound vapour in the gas phase to form an aerosol, which is delivered to a user through the air outlet.

In such preferred embodiments, the housing may further comprise a third compartment downstream of and in communication with the second compartment.

Alternatively or in addition, in such preferred embodiments, the housing may further comprise a mouthpiece in communication with: the second compartment or the third compartment, where included.

The nicotine vapour may react with the volatile delivery enhancing compound vapour in the second compartment to form an aerosol. Where aerosol-generating systems according to the invention further comprise a third compartment downstream of the second compartment, the nicotine vapour may alternatively or in addition react with the volatile delivery enhancing compound vapour in the third compartment to form an aerosol.

The volume of the first compartment and the second compartment may be the same or different. Where aerosol-generating systems according to the invention further comprise a third compartment downstream of the second compartment, the volume of the first compartment, the second compartment and the third compartment may be the same or different.

In certain preferred embodiments, the volume of the first compartment and the second compartment are substantially the same.

In certain embodiments, the volume of the first compartment, the second compartment and the heat transfer barrier are substantially the same.

In one embodiment, the first compartment, the second compartment and the heat transfer barrier are each about 10mm in length.

Where aerosol-generating systems according to the invention comprise a first compartment comprising the nicotine source, the first compartment may be sealed by one or more frangible barriers prior to first use of the aerosol-generating system. In certain preferred

embodiments, the first compartment is sealed by a pair of opposed transverse frangible barriers.

Alternatively or in addition, where aerosol-generating systems according to the invention comprise a second compartment comprising the volatile delivery enhancing compound source, the second compartment may be sealed by one or more frangible barriers prior to first use of the aerosol-generating system. In certain preferred embodiments, the second compartment is sealed by a pair of opposed transverse frangible barriers.

The one or more frangible barriers may be formed from any suitable material. For example, the one or more frangible barriers may be formed from a metal foil or film.

In such embodiments, aerosol-generating systems according to the invention preferably further comprises a piercing element for piercing the one or more frangible barriers sealing one or both of the first compartment and the second compartment prior to first use of the aerosol-generating system. The piercing element may be formed from any suitable material.

Where aerosol-generating systems according to the invention comprise a third compartment, the third compartment may comprise one or more aerosol-modifying agents. For example, the third compartment may comprise one or more sorbents, such as activated carbon, one or more flavourants, such as menthol, or a combination thereof.

Where aerosol-generating systems according to the invention comprise a mouthpiece, the mouthpiece may comprise a filter. The filter may have a low particulate filtration efficiency or very low particulate filtration efficiency. Alternatively, the mouthpiece may comprise a hollow tube.

The heating means of aerosol-generating systems according to the invention may comprise an external heater.

As used herein, the term "external heater" refers to a heater that in use is positioned externally to the nicotine source of the aerosol-generating system.

Alternatively or in addition, the heating means of aerosol-generating systems according to the invention may comprise an internal heater.

As used herein, the term "internal heater" refers to a heater that in use is positioned internally to the nicotine source of the aerosol-generating system.

The heating means may be an electric heating means.

Where the heating means is an electric heating means, the aerosol-generating system may further comprise an electric power supply. Alternatively, the electric heating means may be powered by an external electric power supply.

Where the heating means is an electric heating means, the aerosol-generating system may also further comprise electronic circuitry configured to control the supply of electric power from the electric power supply to the electric heating means. Any suitable electronic circuitry

may be used in order to control the supply of power to the electric heating means. The electronic circuitry may be programmable.

The electric power supply may be a DC voltage source. In preferred embodiments, the electric power supply is a battery. For example, the electric power supply may be a Nickel-metal hydride battery, a Nickel cadmium battery, or a Lithium based battery, for example a
5 Lithium-Cobalt, a Lithium-Iron-Phosphate or a Lithium-Polymer battery. The electric power supply may alternatively be another form of electric charge storage device such as a capacitor. The electric power supply may be rechargeable.

Alternatively, the heating means may be powered by a non-electric power supply, such
10 as a combustible fuel. For example, the heating means may comprise a thermally conductive element that is heated by combustion of a gaseous fuel.

Alternatively, the heating means may be a non-electric heating means, such as a chemical heating means.

In certain embodiments the heating means may comprise a heat sink or heat exchanger
15 configured to transfer thermal energy from an external heat source to the nicotine source. The heat sink or heat exchanger may be formed of any suitable thermally conductive material. Suitable materials include, but are not limited to, metals, such as aluminium and copper.

In certain preferred embodiments, aerosol-generating systems according to the invention may comprise an aerosol-generating article comprising the nicotine source, the volatile delivery
20 enhancing compound source and the heat transfer barrier.

In such embodiments, aerosol-generating systems according to the invention may further comprise an aerosol-generating device in cooperation with the aerosol-generating article, the aerosol generating device comprising the heating means configured to heat the nicotine source of the aerosol-generating article.

As used herein, the term "aerosol-generating article" refers to an article comprising a
25 nicotine source and a delivery enhancing compound source capable of releasing nicotine and a volatile delivery enhancing compound that can react with one another in the gas phase to form an aerosol.

As used herein, the term "aerosol-generating device" refers to a device that interacts
30 with an aerosol-generating article to generate an aerosol that is directly inhalable into a user's lungs thorough the user's mouth.

According to the invention there is also provided an aerosol-generating article for use in an aerosol-generating system according to the invention. According to the invention there is also provided an aerosol-generating device for use in an aerosol-generating system according
35 to the invention.

Preferably, the aerosol-generating article is substantially cylindrical.

The aerosol-generating article may have a transverse cross-section of any suitable

shape.

The aerosol-generating device may comprise a cavity configured to receive the aerosol-generating article.

5 In such embodiments, the cavity of the aerosol-generating device is configured to receive at least the nicotine source of the aerosol-generating article. Preferably, the cavity of the aerosol-generating device is configured to receive the nicotine source, the volatile delivery enhancing compound source and the heat transfer barrier of the aerosol-generating article.

The heating means of the aerosol-generating device may comprise an external heater positioned about a perimeter of the cavity.

10 Alternatively, the heating means of the aerosol-generating device may comprise an internal heater positioned within the cavity.

The heating means of the aerosol-generating device may comprise one or more heating elements. The one or more heating elements may extend partially along the length of the cavity of the aerosol-generating device. The one or more heating elements may extend fully or
15 partially around the circumference of the cavity of the aerosol-generating device.

In a particularly preferred embodiment, the heating means of the aerosol-generating device comprises one or more heating elements comprising an electrically resistive material.

In certain particularly preferred embodiments, aerosol-generating systems according to the invention may comprise an aerosol-generating article comprising a first compartment
20 comprising the nicotine source, a second compartment comprising the volatile delivery enhancing compound source and a heat transfer barrier between the first compartment and the second compartment.

As described above, the aerosol-generating article may comprise one or more frangible barriers sealing one or both of the first compartment and the second compartment.

25 In such embodiments, the aerosol-generating device may comprise a piercing element positioned within the cavity of the aerosol-generating device for piercing the one or more frangible barriers sealing one or both of the first compartment and the second compartment of the aerosol-generating article. The piercing member is preferably positioned centrally within the cavity of the aerosol-generating device, along the longitudinal axis of the cavity.

30 In certain embodiments, the aerosol-generating article may comprise a sealed second compartment comprising a volatile delivery enhancing compound source comprising a tubular porous sorption element and a volatile delivery enhancing compound sorbed on the sorption element and the aerosol-generating device may comprise an elongate piercing element of the type disclosed in WO 2014/140087 A1 comprising a piercing portion adjacent a distal end of the
35 elongate piercing element, a shaft portion, and an obstructing portion adjacent a proximal end of the elongate piercing element. In such embodiments, the piercing portion of the elongate piercing element has a maximum diameter greater than the diameter of the shaft portion of the

elongate piercing element, and the obstructing portion of the elongate piercing element has an outer diameter such that it fits within the tubular porous sorption element of the aerosol-generating article when the aerosol-generating article is received in the aerosol-generating device.

5 In other embodiments, the aerosol-generating device may comprise an elongate piercing element comprising a piercing head at a distal end of the elongate piercing element and a hollow shaft portion comprising at least two apertures wherein, when the aerosol-generating article is received in the aerosol-generating device and the elongate piercing element pierces the one or more frangible barriers sealing one or both of the first compartment and the second
10 compartment of the aerosol-generating article, at least one aperture of the hollow shaft portion of the elongate piercing element is in fluid communication with the first compartment or the second compartment of the aerosol-generating article. In such embodiments, the elongate piercing element has dual functionality: piercing and providing an airflow channel. In certain embodiments, the hollow shaft portion of the elongate piercing element may comprise a first
15 aperture in fluid communication with the first compartment of the aerosol-generating article and a second aperture in fluid communication with the second compartment of the aerosol-generating article.

Preferably, the cavity of the aerosol-generating device is substantially cylindrical.

The cavity of the aerosol-generating device may have a transverse cross-section of any
20 suitable shape. For example, the cavity may be of substantially circular, elliptical, triangular, square, rhomboidal, trapezoidal, pentagonal, hexagonal or octagonal transverse cross-section.

In certain preferred embodiments, the cavity of the aerosol-generating device has a transverse cross-section of substantially the same shape as the transverse cross-section of the aerosol-generating article.

25 In certain particularly preferred embodiments, the cavity of the aerosol-generating device has a transverse cross-section of substantially the same shape and dimensions as the transverse cross-section of the aerosol-generating article.

Preferably, the aerosol-generating article and the cavity of the aerosol-generating device are of substantially circular transverse cross-section or of substantially elliptical transverse
30 cross-section. Most preferably, the aerosol-generating article and the cavity of the aerosol-generating device are of substantially circular transverse cross-section.

Preferably, the length of the cavity of the aerosol-generating device is less than the length of the aerosol-generating article so that when the aerosol-generating article is received in the cavity of the aerosol-generating device the proximal or downstream end of the aerosol-
35 generating article projects from the cavity of the aerosol-generating device.

Preferably, the cavity of the aerosol-generating device has a diameter substantially equal to or slightly greater than the diameter of the aerosol-generating article.

As used herein, by "diameter" is meant the maximum transverse dimension of the aerosol-generating article and the cavity of the aerosol-generating device.

Aerosol-generating systems according to the invention may simulate a smoking article, such as a cigarette, a cigar, a cigarillo or a pipe, or a cigarette pack. In certain preferred
5 embodiments, aerosol-generating systems according to the invention simulate a cigarette.

Where aerosol-generating systems according to the invention comprise an aerosol-generating article, the aerosol-generating article may simulate a smoking article, such as a cigarette, a cigar, a cigarillo or a pipe, or a cigarette pack. In certain preferred embodiments, the aerosol-generating article may simulate a cigarette.

10 For the avoidance of doubt, features described above in relation to one aspect of the invention may also be applicable to other aspects of the invention. In particular, features described above in relation to the first aspect of the invention may also relate, where appropriate, to one or both of the second aspect of the invention and the third aspect of the invention, and vice versa.

15 All scientific and technical terms used herein have meanings commonly used in the art unless otherwise specified. The definitions provided herein are to facilitate understanding of certain terms used frequently herein.

As used herein, the singular forms "a", "an", and "the" encompass embodiments having plural referents, unless the context clearly dictates otherwise.

20 The words "preferred" and "preferably" refer to embodiments of the invention that may afford certain benefits, under certain circumstances. Particularly preferred are aerosol-generating systems according to the invention comprising combinations of preferred features. For example, where aerosol-generating systems according to the invention comprise an aerosol-generating article and an aerosol-generating device in cooperation with the aerosol-
25 generating article, particularly preferred are embodiments comprising a combination of a preferred aerosol-generating article and a preferred aerosol-generating device.

However, it will be appreciated that other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred
30 embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the disclosure and claims.

The invention will now be further described with reference to the accompanying drawing in which:

Figure 1 shows a schematic longitudinal cross-section of an aerosol-generating system according to an embodiment of the invention.

35 Figure 1 schematically shows an aerosol-generating system according to an embodiment of the invention comprising an aerosol-generating article 2 and an aerosol-generating device 4.

The aerosol-generating article 2 has an elongate cylindrical housing comprising a first compartment 6 comprising a nicotine source, a heat transfer barrier 8, a second compartment 10 comprising a volatile delivery enhancing compound source, a third compartment 12 and a mouthpiece 14. As shown in Figure 1, the first compartment 6, the heat transfer barrier 8, the second compartment 10, the third compartment 12 and the mouthpiece 14 are arranged in series and in coaxial alignment within the aerosol-generating article 2. The first compartment 6 is located at the distal end of the aerosol-generating article 2. The second compartment 10 is located downstream of the first compartment 6. The heat transfer barrier 8 is located between the first compartment 6 and the second compartment 10. The third compartment 12 is located immediately downstream of the second compartment 10. The mouthpiece 14 is located immediately downstream of the third compartment 10 at the proximal end of the aerosol-generating article 2.

The upstream and downstream ends of the first compartment 6 and the second compartment 10 of the aerosol-generating article 2 are sealed by frangible aluminium foil barriers (not shown).

The aerosol-generating device 4 comprises a housing comprising an elongate cylindrical cavity in which the aerosol-generating article 2 is received. The length of the cavity is less than the length of the aerosol-generating article 2 so that the proximal end of the aerosol-generating article 2 protrudes from the cavity.

The aerosol-generating device 4 further comprises a power supply 16, a controller (not shown), heating means 18, and a piercing element 20. The power supply 16 is a battery and the controller comprises electronic circuitry and is connected to the power supply 16 and the heating means 18.

The heating means 18 comprises an external heating element positioned about the perimeter of a portion of the cavity at the distal end thereof and extends fully around the circumference of the cavity. As shown in Figure 1, the external heating element is positioned so that it circumscribes the first compartment 6 and an upstream portion of the heat transfer barrier 8 of the aerosol-generating article 2.

The piercing element 20 is positioned centrally within the cavity of the aerosol-generating device 4 and extends along the major axis of the cavity.

In use, as the aerosol-generating article 2 is inserted into the cavity of the aerosol-generating device 4 the piercing element 20 is inserted into the aerosol-generating article 2 and pierces the frangible barriers (not shown) at the upstream and downstream ends of the first compartment 6 and the second compartment 10 of the aerosol-generating article 2. This allows a user to draw air into the housing of the aerosol-generating article through the distal end thereof, downstream through the first compartment 6, the heat transfer barrier 8, the second

compartment 10 and the third compartment 12 and out of the housing through the mouthpiece 14 at the proximal end thereof.

Nicotine vapour is released from the nicotine source in the first compartment 6 into the air stream drawn through the aerosol-generating article 2 and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment 10 into the air stream drawn through the aerosol-generating article 2. The nicotine vapour reacts with the volatile delivery enhancing compound vapour in the gas phase in the second compartment 10 and the third compartment 12 to form an aerosol, which is delivered to the user through the mouthpiece 14 at the proximal end of the aerosol-generating article 2.

In use, the heat transfer barrier 10 reduces heat transfer from the first compartment 6 to the second compartment 10 as the first compartment is heated by the heating means 18 so that the second compartment 10 of the aerosol-generating article 2 is maintained at a lower temperature than the first compartment 6.

The first compartment 6 of the aerosol-generating article 2 comprises a nicotine source comprising a porous sorption element with 10 mg of nicotine sorbed thereon, the heat transfer barrier 8 of the aerosol-generating article 2 comprises an air-filled cavity, and the second compartment 10 of the aerosol-generating article 2 comprises a pyruvic acid source comprising a porous sorption element with 20 mg of pyruvic acid sorbed thereon. The first compartment 6, the heat transfer barrier 8 and the second compartment 10 of the aerosol-generating article 2 are each about 10 mm in length. The third compartment 12 of the aerosol-generating article 2 is about 25 mm in length. The mouthpiece 14 of the aerosol-generating article 2 is about 10 mm in length. The total length of the aerosol-generating article 2 is about 85 mm.

The external heating element of the heating means 18 of the aerosol-generating device 4 is about 15 mm in length. The heating means 18 is configured to heat the first compartment 6 to a temperature of less than about 110°C. In use a constant power supply is provided to the heating means 18 so as to heat the exterior of the first compartment 6 to a temperature of between about 100°C and about 110°C over a period of about 150 seconds and to then maintain the temperature within this range for a period of at least 200 seconds.

Due to inclusion of the heat transfer barrier 8, the second compartment 10 of the aerosol-generating article 2 is maintained at a temperature of less than about 45°C during heating of the first compartment 6 by the heating means 18. To demonstrate this, temperature measurements are taken using first and second temperature sensors during heating of the first compartment 6 by the heating means 18 over a period of 6 minutes starting upon initiation of the heating means 18. The first and second temperature sensors are attached to the exterior of the first and second compartments, respectively, approximately half-way along the length thereof. The results are shown in Table 1.

Time (seconds)	Temperature of first compartment (°C)	Temperature of second compartment (°C)
0	26	25
30	65	25
60	82	27
90	92	30
120	98	33
150	101	35
180	103	37
210	105	38
240	106	39
270	106	40
300	107	41
330	107	42
360	107	43

Table 1

5 The average nicotine delivery ($\mu\text{g}/\text{puff}$) of the aerosol-generating system according to the embodiment of the invention shown in Figure 1 is measured as a function of puff number during operation of the aerosol-generating system according to a Health Canada Intense smoking regime (55cm^3 puff volume, 30 second puff frequency, 2 second puff duration and 100% vent blocking).

10 For the purpose of comparison, the average nicotine delivery ($\mu\text{g}/\text{puff}$) of a reference aerosol-generating system not according to the invention as a function of puff number during operation of the aerosol-generating system according to a Health Canada Intense smoking regime (55cm^3 puff volume, 30 second puff frequency, 2 second puff duration and 100% vent blocking) is also measured. The reference aerosol-generating system differs from the aerosol-

15 generating article according to Figure 1 in that the position of the pyruvic acid source and the nicotine source are reversed such that the first compartment comprises the pyruvic acid source and the second compartment comprises the nicotine source. The aerosol-generating article of the reference aerosol-generating system thus comprises a first compartment comprising a pyruvic acid source comprising a porous sorption element with 20 mg of pyruvic acid sorbed thereon and a second compartment comprising a nicotine source comprising a porous sorption

20 element with 10 mg of nicotine sorbed thereon.

 The average nicotine delivery ($\mu\text{g}/\text{puff}$) of the aerosol-generating system according to the invention, which comprises an aerosol-generating article comprising a nicotine source, a

volatile delivery enhancing compound source downstream of the nicotine source and a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source, increases with increasing puff number. The increasing puff per puff nicotine delivery of the aerosol-generating system according to the invention is similar to the increasing puff per puff nicotine delivery of conventional lit-end cigarettes.

The average nicotine delivery ($\mu\text{g}/\text{puff}$) of the reference aerosol-generating system, which comprises an aerosol-generating article comprising a nicotine source and a volatile delivery enhancing compound immediately upstream of the nicotine source, is significantly lower than the nicotine delivery of the aerosol-generating system according to the invention.

Furthermore, in contrast to the aerosol-generating system according to the invention and conventional lit-end cigarettes, the average nicotine delivery ($\mu\text{g}/\text{puff}$) of the reference aerosol-generating system decreases with increasing puff number.

CLAIMS:

1. An aerosol-generating system comprising:
a nicotine source;
5 a volatile delivery enhancing compound source downstream of the nicotine source,
wherein the volatile delivery enhancing compound comprises an acid;
heating means configured to heat the nicotine source to a temperature of between 80°C
and 150°C; and
a physically separate heat transfer barrier between the nicotine source and the volatile
10 delivery enhancing compound source,
wherein the heat transfer barrier is configured so that in use the temperature of the
volatile delivery enhancing compound source is below 60°C when the nicotine source is heated
to a temperature of between 80°C and 150°C by the heating means.
- 15 2. An aerosol-generating system according to claim 1 wherein the heat transfer barrier
comprises a solid material or a gas, vacuum or partial vacuum or a combination thereof.
3. An aerosol-generating system according to claim 2 wherein the heat transfer barrier
comprises a solid material having a thermal conductivity of less than about 1W per metre Kelvin
20 (W/(m•K)) at 23°C and a relative humidity of 50%.
4. An aerosol-generating system according to claim 2 wherein the heat transfer barrier
comprises a cavity having a length of at least about 8 mm.
- 25 5. An aerosol-generating system according to any preceding claim wherein the nicotine
source comprises a sorption element and nicotine sorbed on the sorption element.
6. An aerosol-generating system according to any preceding claim wherein the volatile
delivery enhancing compound source comprises a sorption element and a volatile delivery
30 enhancing compound sorbed on the sorption element.
7. An aerosol-generating system according to any preceding claim wherein the volatile
delivery enhancing compound comprises a carboxylic acid.
- 35 8. An aerosol-generating system according to claim 7 wherein the acid is selected from the
group consisting of 3-methyl-2-oxovaleric acid, pyruvic acid, 2-oxovaleric acid, 4-methyl-2-

oxovaleric acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid, lactic acid and combinations thereof.

9. An aerosol-generating system according to claim 8 wherein the acid is pyruvic acid or lactic acid.

10. An aerosol-generating system according to any preceding claim comprising a housing comprising an air inlet and an air outlet, the housing comprising in series from air inlet to air outlet:

a first compartment comprising the nicotine source in communication with the air inlet;
a second compartment comprising the volatile delivery enhancing compound source in communication with the first compartment; and
a physically separate heat transfer barrier between the first compartment and the second compartment,

wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

11. An aerosol-generating system according to claim 10 wherein one or both of the first compartment and the second compartment are sealed by one or more frangible seals.

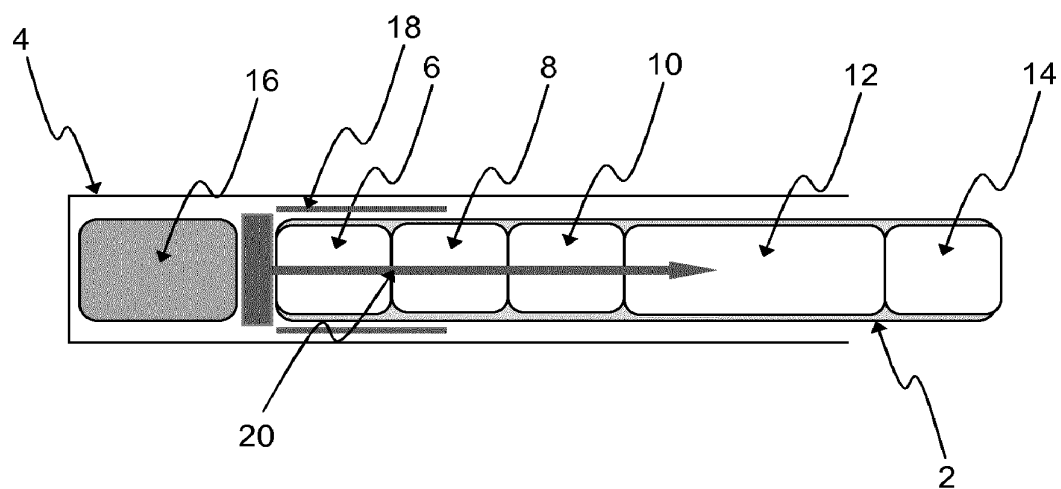
12. An aerosol-generating system according to claim 11 further comprising a piercing element for piercing the one or more frangible barriers sealing one or both of the first compartment and the second compartment.

13. An aerosol-generating system according to any preceding claim comprising:
an aerosol-generating article comprising the nicotine source, the volatile delivery enhancing compound source and the heat transfer barrier.

14. An aerosol-generating system according to claim 13 further comprising:
an aerosol-generating device in cooperation with the aerosol-generating article, the aerosol generating device comprising the heating means configured to heat the nicotine source of the aerosol-generating article.

15. An aerosol-generating article for use in an aerosol-generating system according to claim 13 or 14.

- 1/1 -

**Figure 1**

(51) International Patent Classification:
A24F 47/00 (2006.01)(21) International Application Number:
PCT/EP2014/070034(22) International Filing Date:
19 September 2014 (19.09.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
13185245.1 19 September 2013 (19.09.2013) EP(71) Applicant: PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).(72) Inventors: ZUBER, Gérard; Route du Chalet à Gobet 2,
CH-1055 Froideville (CH). FARINE, Marie; Chemin du
Chablais 102, CH-1786 Sugiez (CH). SILVESTRINI,
Patrick Charles; Chemin de Maujobia 145, CH-2000
Neuchâtel (CH).(74) Agent: MILLBURN, Julie; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))(88) Date of publication of the international search report:
11 June 2015

(54) Title: AEROSOL-GENERATING SYSTEM FOR GENERATING NICOTINE SALT PARTICLES

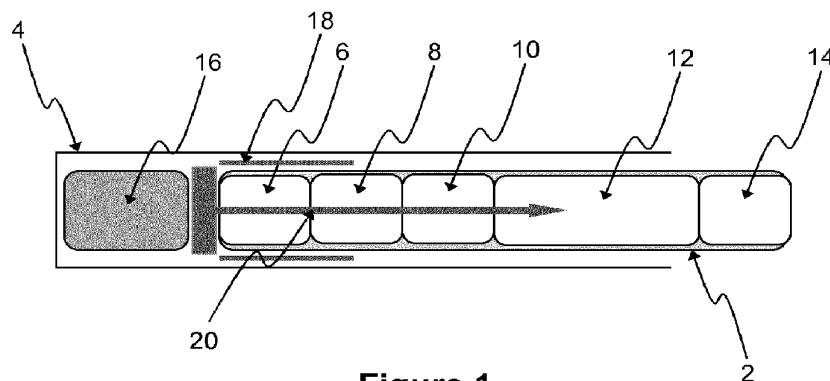


Figure 1

(57) Abstract: An aerosol-generating system comprises: a nicotine source (6); a volatile delivery enhancing compound source (10) downstream of the nicotine source, wherein the volatile delivery enhancing compound comprises an acid; heating means (18) for heating the nicotine source; and a physically separate heat transfer barrier (8) between the nicotine source and the volatile delivery enhancing compound source. The heating means is preferably configured to heat the nicotine source to a temperature of between about 80°C and about 150°C. The heat transfer barrier is preferably configured so that in use the temperature of the volatile delivery enhancing compound source is less than about 50°C when the nicotine source is heated to a temperature of between 80°C and 150°C by the heating means. The heat transfer barrier may comprise a solid material having a thermal conductivity of less than about 1W per metre Kelvin (W/(m•K)) at 23°C and a relative humidity of 50%. Alternatively, the heat transfer barrier may comprise a cavity having a length of at least about 8mm.

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/070034

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24F47/00

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 520 231 A2 (REYNOLDS TOBACCO CO R [US]) 30 December 1992 (1992-12-30) page 6, line 28 - page 13, line 52 -----	1
A	WO 2008/121610 A1 (UNIV DUKE [US]; ROSE JED E [US]; ROSE SETH D [US]; TURNER JAMES EDWARD) 9 October 2008 (2008-10-09) cited in the application paragraph [0133] - paragraph [0150] paragraph [0221] - paragraph [0255] -----	1
A	DE 10 2011 111999 A1 (KRAPF RAINER [DE]) 28 February 2013 (2013-02-28) paragraph [0091] - paragraph [0102] -----	1



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

8 January 2015

Date of mailing of the international search report

22/04/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Koob, Michael

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2014/070034

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-14

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-14

An aerosol-generating system comprising a nicotine source, a volatile delivery enhancing compound source downstream of the nicotine source, wherein the volatile delivery enhancing compound comprises an acid, heating means configured to heat the nicotine source to a temperature of between about 80°C and about 150°C and a physically separate heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source, wherein the heat transfer barrier is configured so that in use the temperature of the volatile delivery enhancing compound source is below about 60°C when the nicotine source is heated to a temperature of between 80°C and 150°C by the heating means.

2. claim: 15

An aerosol-generating article comprising the nicotine source, the volatile delivery enhancing compound source and the heat transfer barrier for use in the system of the first invention.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/070034

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0520231	A2	30-12-1992	CA 2069687 A1 29-12-1992
			EP 0520231 A2 30-12-1992
			JP H05184675 A 27-07-1993
			US 5538020 A 23-07-1996
			US 5593792 A 14-01-1997

WO 2008121610	A1	09-10-2008	AU 2008232897 A1 09-10-2008
			CA 2682432 A1 09-10-2008
			CN 102014995 A 13-04-2011
			CN 103418062 A 04-12-2013
			EP 2134395 A1 23-12-2009
			EP 2708256 A2 19-03-2014
			JP 2010532672 A 14-10-2010
			JP 2013144157 A 25-07-2013
			US 2008241255 A1 02-10-2008
			WO 2008121610 A1 09-10-2008

DE 102011111999	A1	28-02-2013	DE 102011111999 A1 28-02-2013
			WO 2013030202 A1 07-03-2013



(51) International Patent Classification:
A24F 47/00 (2006.01)

(21) International Application Number:
PCT/EP2014/076650

(22) International Filing Date:
4 December 2014 (04.12.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
13195953.8 5 December 2013 (05.12.2013) EP

(71) Applicant: PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).

(72) Inventor: ZUBER, Gerard; Route du Chalet a Gobet 2,
CH-1055 Froideville (CH).

(74) Agent: BATES, Alan; 16 Theobalds Road, London Great-
er London WC1X 8PL (GB).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: NON-TOBACCO NICOTINE-CONTAINING ARTICLE

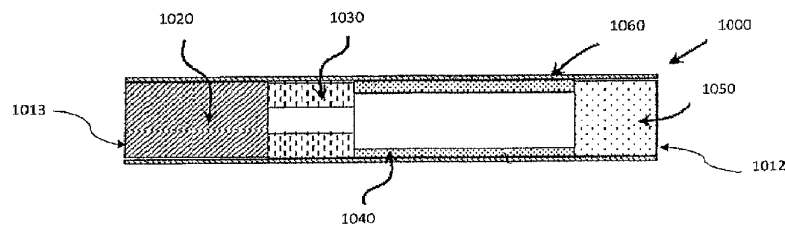


FIGURE 2

(57) Abstract: An aerosol-generating rod comprises a gathered sheet of non-tobacco material circumscribed by a wrapper. The sheet of non-tobacco material comprises a sorbent substrate such as paper, a nicotine salt, and an aerosol-former. The sheet of non-tobacco material is textured or crimped. An aerosol-generating article may comprise the aerosol-generating rod as a component element.

WO 2015/082652 A1

NON-TOBACCO NICOTINE-CONTAINING ARTICLE

The present specification relates to aerosol-generating rods comprising gathered sheets of a non-tobacco nicotine-bearing material for use in aerosol-generating articles. The specification also relates to aerosol-generating articles comprising such aerosol-generating rods as aerosol-forming substrates.

So-called 'e-cigarettes' and other electrically operated smoking systems that vaporise a liquid nicotine formulation to form an aerosol that is inhaled by a user are known in the art. For example, WO 2009/132793 A1 discloses an electrically heated smoking system comprising a shell and a replaceable mouthpiece wherein the shell comprises an electric power supply and electric circuitry. The mouthpiece comprises a liquid storage portion, a capillary wick having a first end that extends into the liquid storage portion for contact with liquid therein, and a heating element for heating a second end of the capillary wick. In use, liquid is transferred from the liquid storage portion towards the heating element by capillary action in the wick. Liquid at the second end of the wick is vaporised by the heating element.

Most current commercial e-cigarettes or electronic nicotine delivery systems (ENDSs) fail to deliver more than 50 µg nicotine per puff, under the Health Canada intense smoking regime. Typically, the mean nicotine delivery per puff for ENDSs ranges from 20 to 30 µg nicotine per puff. A few studies report that ENDSs deliver little nicotine to the blood. Nicotine pharmacokinetics data on naïve or first time ENDS users show very low plasma nicotine concentrations in the range of 0.5 ng/mL to 3.5 ng/mL, which compares to typical plasma nicotine concentrations resulting from tobacco cigarette smoking of 10 to 20 ng/mL. However, a more recent study on "experienced" ENDS users (i.e. users who had been using ENDS for about 1 year) indicated a significant increase in plasma nicotine concentration ($C_{max} = 10.3$ ng/mL), which almost matches pharmacokinetic data of conventional cigarette smokers. The explanation of this observed discrepancy in plasma nicotine concentrations between "naïve" and "experienced" ENDS users may be that, as recent studies have shown, average puff duration is significantly longer for "experienced" ENDS users (puff duration = 4.2 ± 0.7 s) in comparison to "naïve" ENDS users (puff duration = 2.4 ± 0.5 s). This is believed to be because "naïve" ENDS users have the tendency to smoke ENDS in the same way as a conventional tobacco cigarette (puff duration = 2.1 ± 0.4 s). Because they take longer and deeper puffs, "experienced" ENDS users may reach nicotine deliveries and plasma nicotine levels similar to the levels reached by conventional tobacco cigarette smokers.

Further studies have shown that the vast majority of experienced ENDS users use e-cigarette models that are generally large in size, with high battery power. Based on these recent studies, it appears that long-term ENDS users are opting for more powerful devices, such as tank systems, with higher nicotine deliveries and are adapting their "vaping" topography in order to

reach plasma nicotine levels similar to tobacco cigarette smoking. The adaptation to a new smoking/vaping ritual may be cumbersome for some ENDS users and may have implications in the formation of undesirable compounds. For example, longer puff durations and greater puff volumes may induce the phenomena of "dry puff".

Furthermore, commercial e-cigarettes involve the use of a liquid nicotine containing substrate. The handling of such liquids may be cumbersome or undesirable for an end user.

It would be desirable to provide rods comprising non-tobacco nicotine-bearing material for use in aerosol-generating articles. It would further be desirable to provide aerosol-generating articles that provide a similar nicotine delivery to conventional cigarettes without the need to use bulky aerosol-generating devices.

An aerosol-generating rod may be provided comprising a gathered sheet of non-tobacco material circumscribed by a wrapper. The sheet of non-tobacco material is textured or crimped and comprises a sorbent substrate, a nicotine salt, and an aerosol-former. The gathered sheet of material non-tobacco preferably extends along substantially the entire length of the aerosol-generating rod and across substantially the entire transverse cross-sectional area of the aerosol-generating rod. The sheet may further comprise water.

The sheet may further comprise a flavourant. The flavourant may comprise a volatile flavour component. The flavourant may comprise menthol. As used herein, the term 'menthol' denotes the compound 2-isopropyl-5-methylcyclohexanol in any of its isomeric forms. The flavourant may provide a flavour selected from the group consisting of menthol, lemon, vanilla, orange, wintergreen, cherry, and cinnamon.

As the nicotine and aerosol former are absorbed or coated onto a sorbent substrate, an aerosol-generating article comprising the aerosol-generating rod does not comprise flowable liquid. Thus, an end user need not be concerned with handling of liquid formulations. Furthermore, the nicotine salts may produce a nicotine bearing aerosol at low temperatures compared with heated aerosol generating articles that heat a tobacco substrate. Thus, an aerosol-generating rod may form a nicotine bearing aerosol when heated to temperatures lower than 300 °C, for example lower than 250 °C, or lower than 220 °C. A nicotine bearing aerosol may be generated at temperatures as low as 120-140 °C. Thus, there is no need to use a cumbersome aerosol generating device to generate an aerosol with high levels of nicotine.

Preferably the sheet of non-tobacco material comprises one or more nicotine salt selected from the list consisting of nicotine citrate, nicotine pyruvate, nicotine bitartrate, nicotine pectates, nicotine aginates, and nicotine salicylate. Nicotine in these salt forms is more stable than liquid freebase nicotine typically used in e-cigarettes. Thus, aerosol-generating articles comprising the aerosol-generating rods may have longer shelf lives than typical e-cigarettes.

As used herein, an "aerosol former" is any suitable known compound or mixture of compounds that, in use, facilitates formation of a dense and stable aerosol and that is substantially

resistant to thermal degradation at the operating temperature of the aerosol-generating article. Suitable aerosol-formers are well known in the art and include, but are not limited to: polyhydric alcohols, such as triethylene glycol, 1,3-butanediol and glycerine; esters of polyhydric alcohols, such as glycerol mono-, di- or triacetate; and aliphatic esters of mono-, di- or polycarboxylic acids, such as dimethyl dodecanedioate and dimethyl tetradecanedioate. Preferred aerosol formers are polyhydric alcohols or mixtures thereof, such as triethylene glycol, 1,3-butanediol and, most preferred, glycerine,

Preferably, the aerosol former is one or more aerosol former selected from the list consisting of propylene glycol, triethylene glycol, 1,3-butanediol, and glycerine.

The nicotine and the aerosol-former may be combined with water as a liquid formulation. The liquid formulation may further comprise a flavourant. Such a liquid formulation may then be absorbed by a sorbent substrate or coated onto the surface of a substrate.

The sorbent substrate may be a sheet of cellulosic-based material onto which the nicotine salt and the aerosol former may be coated or absorbed. For example, the sorbent substrate may be a sheet of paper.

Preferably the ratio of aerosol-former to nicotine in the sheet of non-tobacco material is lower than 15:1. For example, the ratio of aerosol-former to nicotine in the sheet of non-tobacco material may be between 3:1 and 10:1, for example about 4:1, or 5:1, or 6:1. E-cigarettes typically utilize a liquid aerosol-forming substrate that has an aerosol former to nicotine ratio in the range between 20:1 and 100:1. On heating such formulations, an aerosol may be developed that has a low nicotine concentration. This may, in turn, result in users drawing deeper and longer puffs to provide a desired nicotine intake.

The aerosol-generating rod may comprise at least one further sheet of material, the further sheet of material gathered together with the sheet of non-tobacco material and circumscribed by the wrapper. The further sheet may comprise a flavourant. The further sheet may be a thermally conductive material to improve thermal transfer through the aerosol-generating rod. The further sheet may be or comprise a material that is susceptible to induction to allow it to be used in inductive heating of the aerosol-generating rod. The further sheet may be a metal foil, for example aluminium foil.

The aerosol-generating rod may comprise one or more susceptor elements for inductive heating. Such susceptor elements may be incorporated into the aerosol-generating rod as threads or wires of suitable susceptor material. Such susceptor elements may be incorporated on or in the sheet of non-tobacco material, for example susceptor elements may be printed onto a surface of the sheet of non-tobacco material.

As used herein, the term 'rod' is used to denote a generally cylindrical element of substantially circular, oval or elliptical cross-section.

As used herein, the term 'sheet' denotes a laminar element having a width and length substantially greater than the thickness thereof. The width of a sheet is greater than 10 mm, preferably greater than 20 mm or 30 mm.

As used herein, the term "aerosol-forming material" denotes a material that is capable of releasing volatile compounds upon heating to generate an aerosol. An aerosol-forming substrate may comprise or consist of an aerosol-forming material.

As used herein, the term 'aerosol-generating rod' is used to denote a generally cylindrical element of substantially circular, oval or elliptical cross-section that comprises or consists of an aerosol-forming material.

As used herein, the term 'rod length' denotes the dimension in the direction of the cylindrical axis of rods as described herein.

As used herein, the term 'gathered' denotes that the sheet of tobacco material is convoluted, folded, or otherwise compressed or constricted substantially transversely to the cylindrical axis of the rod.

As used herein, the terms 'upstream' and 'downstream' are used to describe the relative positions of components, or portions of components, of aerosol-generating articles comprising rods as described herein in relation to the direction of air drawn through the aerosol-generating articles during use thereof.

The aerosol-generating rods comprise a gathered textured sheet of non-tobacco nicotine-bearing material circumscribed by a wrapper. Use of a textured sheet of material may advantageously facilitate gathering of the sheet to form an aerosol-generating rod.

As used herein, the term 'textured sheet' denotes a sheet that has been crimped, embossed, debossed, perforated or otherwise deformed. Textured sheets material may comprise a plurality of spaced-apart indentations, protrusions, perforations or a combination thereof.

As used herein, the term 'crimped sheet' is intended to be synonymous with the term 'creped sheet' and denotes a sheet having a plurality of substantially parallel ridges or corrugations. Preferably, the crimped sheet of material has a plurality of ridges or corrugations substantially parallel to the cylindrical axis of the aerosol-generating rod. This advantageously facilitates gathering of the crimped sheet of material to form the aerosol-generating rod.

Sheets of non-tobacco material for use in the production of aerosol-generating rods may be textured using suitable known machinery for texturing filter tow, paper and other materials.

Sheets of non-tobacco material for use in the invention may be crimped using a crimping unit of the type described in CH-A-691156, which comprises a pair of rotatable crimping rollers. However, it will be appreciated that sheets of non-tobacco material may be textured using other suitable machinery and processes that deform or perforate the sheets material.

Aerosol-generating rods may be produced using conventional cigarette filter making machinery.

For example, rods comprising a gathered crimped sheet of non-tobacco material may be produced using machinery for forming filter rods comprising a gathered crimped sheet of paper of the type described in CH-A-691156.

A method of forming an aerosol-generating rod may comprising the steps of: providing a continuous sheet of non-tobacco material; gathering the continuous sheet of non-tobacco material transversely relative to the longitudinal axis thereof; circumscribing the gathered continuous sheet of non-tobacco material with a wrapper to form a continuous rod; and severing the continuous rod into a plurality of discrete aerosol-generating rods. The non-tobacco material comprises a sorbent substrate, a nicotine salt, and an aerosol former.

The method may further comprise the step of coating the sorbent substrate with the nicotine salt and the aerosol-former. The method may comprise the step of absorbing the nicotine salt and the aerosol-former into the sorbent substrate. Preferably, aerosol-generating rods as described herein are of substantially uniform cross-section.

Aerosol-generating rods as described herein for use as aerosol-forming substrates in heated aerosol-generating articles may typically have a rod length of between about 5 mm and about 20 mm or about 30 mm.

Preferably, sheets of material for use in forming aerosol-generating rods as described herein have a width of at least about 25 mm.

In certain embodiments sheets of material for use in aerosol-generating rods as described herein may have a width of between about 25 mm and about 300 mm.

Preferably, the sheets of material that make up the aerosol-generating rod have a thickness of at least about 50 μm to about 300 μm .

Aerosol-generating rods as described herein may comprise a gathered sheet of non-tobacco material circumscribed by a porous wrapper or a non-porous wrapper.

An aerosol-generating rod as described may be particularly beneficial as a component of an aerosol-generating article, particularly a heated aerosol-generating article. A preferred use of an aerosol-generating rod as described above is as an aerosol-forming substrate of a heated aerosol-generating article. An aerosol-generating article may be provided comprising an aerosol-generating rod as described above as a component element.

Heated aerosol-generating systems operate by heating an aerosol-forming substrate to generate an aerosol from the substrate. The aerosol can then be inhaled by a consumer. On heating a substrate comprising an aerosol-generating rod as described herein, an inhalable aerosol comprising nicotine and an aerosol-former is generated.

A number of aerosol-generating articles in which an aerosol-forming substrate is heated rather than combusted have been proposed in the art. Typically in heated aerosol-generating articles, an aerosol is generated by the transfer of heat from a heat source, for example a

chemical, electrical or combustible heat source, to a physically separate aerosol-generating substrate, which may be located within, around or downstream of the heat source.

As used herein, the term 'aerosol-generating substrate' denotes a substrate formed from or comprising an aerosol-forming material that is capable of releasing volatile compounds upon heating to generate an aerosol.

In one embodiment, aerosol-generating rods as described herein may be used as aerosol-generating substrates in heated aerosol-generating articles comprising a combustible heat source and an aerosol-generating substrate downstream of the combustible heat source.

For example, aerosol-generating rods as described herein may be used as aerosol-generating substrates in heated aerosol-generating articles of the type disclosed in WO-A-2009/022232, which comprise a combustible carbon-based heat source, an aerosol-generating substrate downstream of the combustible heat source, and a heat-conducting element around and in contact with a rear portion of the combustible carbon-based heat source and an adjacent front portion of the aerosol-generating substrate. However, it will be appreciated that aerosol-generating rods as described herein may also be used as aerosol-generating substrates in heated aerosol-generating articles comprising combustible heat sources having other constructions.

In another embodiment, aerosol-generating rods as described herein may be used as aerosol-generating substrates in heated aerosol-generating articles for use in electrically-operated aerosol-generating systems in which the aerosol-generating substrate of the heated aerosol-generating article is heated by an electrical heat source.

For example, aerosol-generating rods as described herein may be used as aerosol-generating substrates in heated aerosol-generating articles of the type disclosed in EP-A-0 822 670.

An aerosol generating rod may be one of a number of component elements of an aerosol-generating article. For example, an aerosol-generating article may comprise an aerosol-generating rod as described herein and one or more other elements assembled within a cigarette paper. The one or more other elements may include a mouthpiece, an aerosol-cooling element, an a support element such as a hollow acetate tube. In one embodiment an aerosol-generating article may comprise, in a linear sequential arrangement, an aerosol-forming substrate formed from an aerosol-generating rod, a support element located immediately downstream of the aerosol-forming substrate, an aerosol-cooling element located downstream of the support element, and an outer wrapper circumscribing the aerosol-forming substrate, the support element and the aerosol-cooling element. The aerosol-forming substrate may be penetrable by the heating element of an aerosol-generating device.

A system may be provided comprising an electrically-operated aerosol-generating device or apparatus and an aerosol-generating article for use with the apparatus. The aerosol-generating article comprises an aerosol-generating rod as described herein. The aerosol-generating device

may comprise a heating element designed to be inserted into the aerosol-generating article. The aerosol-generating device may comprise a heating element designed to surround a portion of the aerosol-generating article. In certain embodiments of a system, the aerosol-generating device may comprise an induction element for inductively heating a susceptor comprised in the aerosol-

5 generating article.

Specific embodiments will be further described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 shows a schematic cross-section of apparatus for forming an aerosol-generating rod according to a specific embodiment;

10 Figures 2, 3, and 4 illustrate embodiments of aerosol-generating articles that incorporate aerosol-generating rods formed as described herein;

Figure 5 illustrates an aerosol-generating system comprising an electrically-operated aerosol-generating device and an aerosol-generating article as illustrated in Figure 2; and

Figure 6 is a schematic cross-sectional diagram of the electrically-operated aerosol-

15 generating device illustrated in Figure 5.

The apparatus shown in Figure 1 generally comprises: supply means for providing a continuous sheet of non-tobacco; crimping means for crimping the continuous sheet; rod forming means for gathering the continuous crimped sheet and circumscribing the gathered material with a wrapper to form a continuous rod; and cutting means for severing the continuous rod into a plurality of discrete aerosol-generating rods. The apparatus also comprises transport means for transporting the continuous sheet of material downstream through the apparatus from the supply means to the rod forming means via the crimping means.

20

As shown in Figure 1, the supply means for providing a continuous sheet comprises a continuous sheet of non-tobacco 2 mounted on a bobbin 4. The non-tobacco material is a cigarette paper that has been soaked in a liquid formulation comprising nicotine pyruvate, glycerine, and water. The cigarette paper absorbs the liquid formulation and the non-tobacco sheet thus comprises nicotine pyruvate, glycerine and water. The ratio of glycerine to nicotine is 5:1.

25

The crimping means comprises a pair of rotatable crimping rollers 6. In use, the continuous sheet of non-tobacco material 2 is drawn from the first bobbin 4 and transported downstream to the pair of crimping rollers 6 by the transport mechanism via a series of guide and tensioning rollers. As the continuous sheet of non-tobacco material 2 is fed between the pair of crimping rollers 6, the crimping rollers engage and crimp the sheet 2 to form a continuous crimped sheet 8 having a plurality of spaced-apart ridges or corrugations substantially parallel to the longitudinal axis of the sheet through the apparatus.

30

35

The continuous crimped sheet 8 is transported downstream from the pair of crimping rollers 6 towards the rod forming means and fed through a converging funnel or horn 10. The converging

funnel 10 gathers the continuous sheet 8 transversely relative to its longitudinal axes. The sheet of material 8 assumes a substantially cylindrical configuration as it passes through the converging funnel 10.

Upon exiting the converging funnel 10, the gathered sheet of non-tobacco material is wrapped in a continuous sheet of wrapper material 12. The wrapper is a paper wrapper and is fed from a bobbin 14 and enveloped around the gathered continuous crimped sheet by an endless belt conveyor or garniture. As shown in Figure 1, the rod forming means comprises an adhesive application means 16 that applies adhesive to one of the longitudinal edges of the wrapper, so that when the opposed longitudinal edges of the wrapper are brought into contact they adhere to one other to form a continuous rod.

The rod forming means further comprises a drying means 18 downstream of the adhesive application means 16, which in use dries the adhesive applied to the seam of the continuous rod as the continuous rod is transported downstream from the rod forming means to the cutting means.

The cutting means comprises a rotary cutter 20 that severs the continuous rod into a plurality of discrete aerosol-forming rods of unit rod length or multiple unit rod length.

Figure 2 illustrates an embodiment of a heated aerosol-generating article 1000 comprising an aerosol-generating rod as described herein. The article 1000 comprises four elements; an aerosol-forming substrate 1020 comprising the aerosol-generating rod, a hollow cellulose acetate tube 1030, a spacer element 1040, and a mouthpiece filter 1050. These four elements are arranged sequentially and in coaxial alignment and are assembled by a cigarette paper 1060 to form the aerosol-generating article 1000. The article 1000 has a mouth-end 1012, which a user inserts into his or her mouth during use, and a distal end 1013 located at the opposite end of the article to the mouth end 1012. The embodiment of an aerosol-generating article illustrated in Figure 2 is particularly suitable for use with an electrically-operated aerosol-generating device comprising a heater for heating the aerosol-forming substrate.

When assembled, the article 1000 is about 45 millimetres in length and has an outer diameter of about 7.2 millimetres.

The aerosol-forming substrate 1020 comprises an aerosol-generating rod formed from a crimped and gathered sheet of nicotine pyruvate and glycerin bearing paper.

An aerosol-generating article 1000 as illustrated in Figure 2 is designed to engage with an aerosol-generating device in order to be consumed. Such an aerosol-generating device includes means for heating the aerosol-forming substrate 1020 to a sufficient temperature to form an aerosol. Typically, the aerosol-generating device may comprise a heating element that surrounds the aerosol-generating article 1000 adjacent to the aerosol-forming substrate 1020, or a heating element that is inserted into the aerosol-forming substrate 1020.

Once engaged with an aerosol-generating device, a user draws on the mouth-end 1012 of the smoking article 1000 and the aerosol-forming substrate 1020 is heated to a temperature of

about 220 degrees Celsius. At this temperature an aerosol comprising nicotine pyruvate, glycerine, and water is evolved. The aerosol is drawn through the filter 1050 and into the user's mouth. It is noted that the temperature that the substrate is heated to is considerably lower than the temperature that would be required to evolve an aerosol from a tobacco substrate.

5 Figure 3 illustrates an alternative embodiment of an aerosol-generating article 5000. The aerosol-generating article 5000 comprises four elements arranged in coaxial alignment: an aerosol-forming substrate 5020, a support element 5030, an aerosol-cooling element 5040, and a mouthpiece 5050. These four elements are arranged sequentially and are circumscribed by an outer wrapper 5060 to form the aerosol-generating article 5000. The aerosol-cooling element 5040
10 acts as a spacer element as described in relation to Figure 2 as well as an aerosol-cooling element. In use, volatile substances released from the aerosol-forming substrate 5020 pass along the aerosol-cooling element 5040 towards a mouth end 5070 of the aerosol-generating article 5000. The volatile substances may cool within the aerosol-cooling element 5040 to form an aerosol that is inhaled by the user. In the embodiment illustrated in Figure 5, the aerosol-cooling
15 element comprises a crimped and gathered sheet of polylactic acid circumscribed by a wrapper. The aerosol-forming substrate 5020 comprises an aerosol-generating rod formed from a crimped and gathered sheet of nicotine pyruvate and glycerin bearing paper. The aerosol-generating article 5000 has a proximal or mouth end 5070, which a user inserts into his or her mouth during use, and a distal end 5080 located at the opposite end of the aerosol-generating article 5000 to the
20 mouth end 5070.

Figure 4 illustrates a second embodiment of an aerosol-generating article 1001. While the article of Figure 2 or Figure 3 is intended to be consumed in conjunction with an aerosol-generating device, the article of Figure 4 comprises a combustible heat source 1080 that may be ignited and transfer heat to the aerosol-forming substrate 1020 to form an inhalable aerosol. The combustible
25 heat source 1080 is a charcoal element that is assembled in proximity to the aerosol-forming substrate at a distal end 1013 of the article 1001. Elements that are essentially the same as elements in Figure 2 have been given the same numbering as the article in Figure 2.

Figure 5 illustrates a portion of an electrically-operated aerosol-generating system 2000 that utilises a heating blade 2100 to heat an aerosol-generating substrate 1020 of an aerosol-
30 generating article 1000. The heating blade is mounted within an aerosol article receiving chamber of an electrically-operated aerosol-generating device 2010. The aerosol-generating device defines a plurality of air holes 2050 for allowing air to flow to the aerosol-generating article 1000. Air flow is indicated by arrows on Figure 5. The aerosol-generating device comprises a power supply and electronics, which are not illustrated in Figure 5. The aerosol-generating article 1000 of Figure 5 is
35 as described in relation to Figure 2.

In Figure 6, the components of the aerosol-generating device 2010 are shown in a simplified manner. Particularly, the components of the aerosol-generating device 2010 are not

drawn to scale in Figure 6. Components that are not relevant for the understanding of the embodiment have been omitted to simplify Figure 6.

As shown in Figure 6, the aerosol-generating device 2010 comprises a housing 6130. The heating element 6120 is mounted within an aerosol-generating article receiving chamber within the housing 6130. The aerosol-generating article 1000 (shown by dashed lines in Figure 5) is inserted into the aerosol-generating article receiving chamber within the housing 6130 of the aerosol-generating device 2010 such that the heating element 6120 is directly inserted into the aerosol-forming substrate 1020 of the aerosol-generating article 1000.

Within the housing 6130 there is an electrical energy supply 6140, for example a rechargeable lithium ion battery. A controller 6150 is connected to the heating element 6120, the electrical energy supply 6140, and a user interface 6160, for example a button or display. The controller 6150 controls the power supplied to the heating element 6120 in order to regulate its temperature.

The exemplary embodiments described above are not limiting. In view of the above-discussed exemplary embodiments, other embodiments consistent with the above exemplary embodiment will now be apparent to one of ordinary skill in the art.

CLAIMS:

1. An aerosol-generating rod comprising a gathered sheet of non-tobacco material circumscribed by a wrapper, in which the sheet of non-tobacco material is textured or crimped and comprises a sorbent substrate, a nicotine salt, and an aerosol-former.
- 5 2. An aerosol-generating rod according to claim 1 in which the sheet of non-tobacco material further comprises water.
3. An aerosol-generating rod according to claim 1 or 2 in which the sheet of non-tobacco material further comprises a flavourant.
- 10 4. An aerosol-generating rod according to claim 1, 2, or 3 in which the sheet of non-tobacco material comprises one or more nicotine salt selected from the list consisting of nicotine citrate, nicotine pyruvate, nicotine bitartrate, and nicotine salicylate.
5. An aerosol-generating rod according to any preceding claim in which the aerosol former is one or more aerosol former selected from the list consisting of propylene glycol, triethylene glycol, 1,3-butanediol, and glycerine.
- 15 6. An aerosol-generating rod according to any preceding claim comprising a menthol flavourant.
7. An aerosol-generating rod according to any preceding claim further comprising a further sheet of material, gathered together with the sheet of non-tobacco material and circumscribed by the wrapper.
- 20 8. An aerosol-generating rod according to any preceding claim further comprising an inductive susceptor gathered together with the sheet of non-tobacco material and circumscribed by the wrapper.
9. An aerosol-generating rod according to any preceding claim in which the sorbent substrate is a sheet of cellulosic-based material onto which the nicotine salt and the aerosol former may be coated or absorbed.
- 25 10. An aerosol-generating rod according to any preceding claim in which the ratio of aerosol-former to nicotine in the sheet of non-tobacco material is between 3:1 and 10:1.
11. An aerosol-generating article comprising an aerosol-forming substrate, in which the aerosol-forming substrate is an aerosol-generating rod according to any of claims 1 to 10.
- 30 12. A system comprising an electrically-operated aerosol-generating apparatus and an aerosol-generating article for use with the apparatus, the aerosol-generating article comprising an aerosol-forming substrate in the form of an aerosol-generating rod according to any of claims 1 to 10.
- 35 13. A heated aerosol-generating article comprising a combustible heat source and an aerosol-forming substrate located downstream of the combustible heat source, in which the aerosol-forming substrate is an aerosol-generating rod according to any of claims 1 to 10.

14. A heated aerosol-generating article for use in an electrically-operated aerosol-generating system comprising an aerosol-forming substrate, in which the aerosol-forming substrate is an aerosol-generating rod according to any of claims 1 to 10.

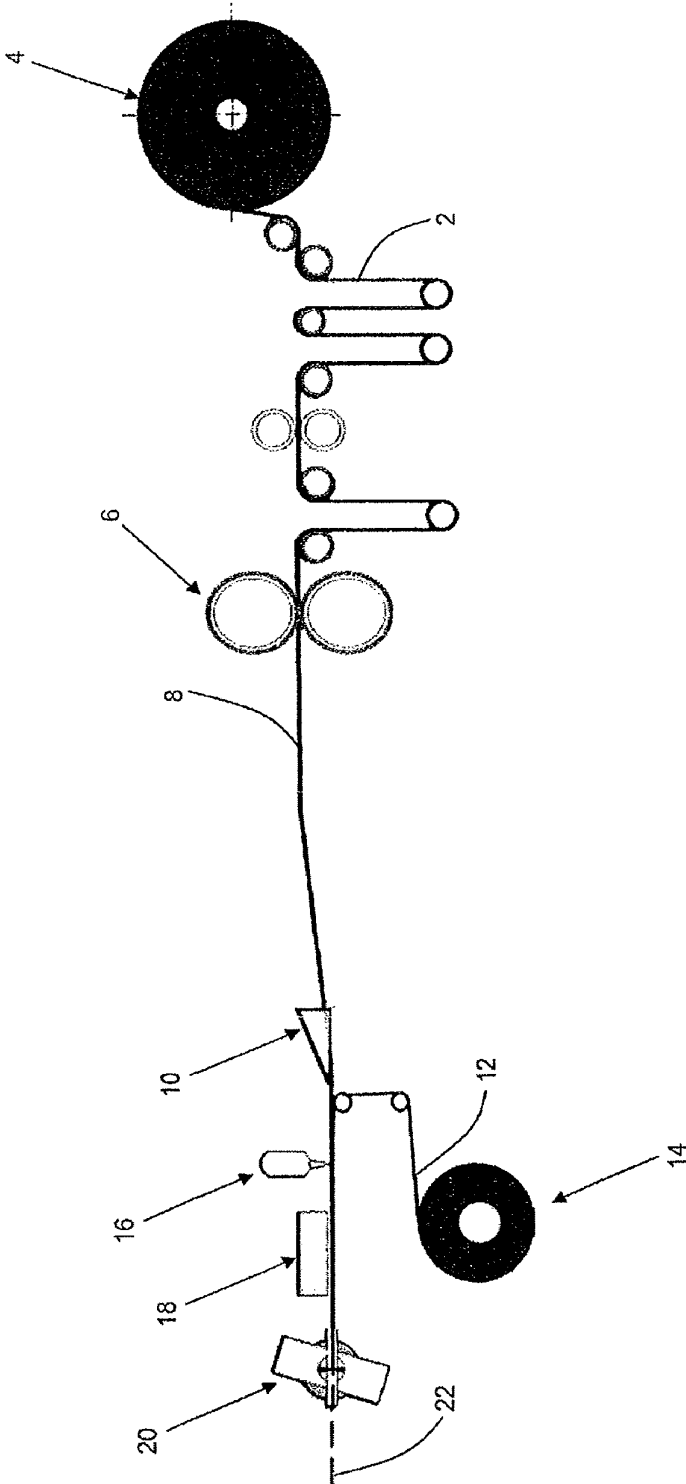


FIGURE 1

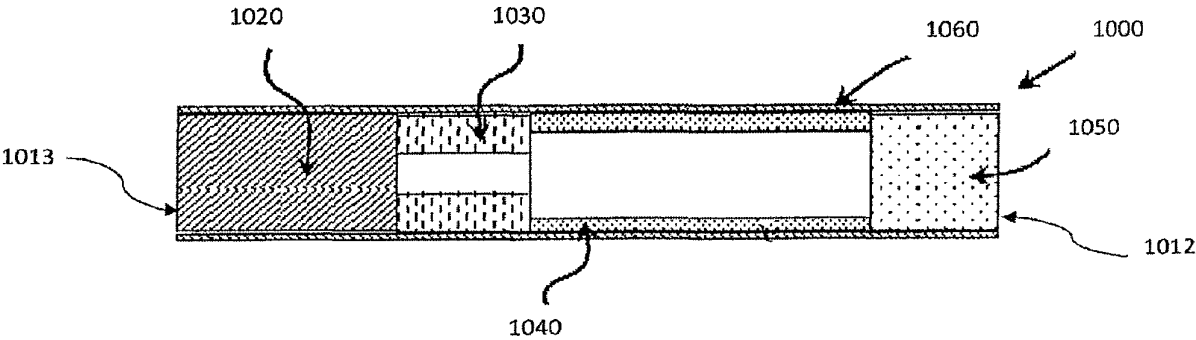


FIGURE 2

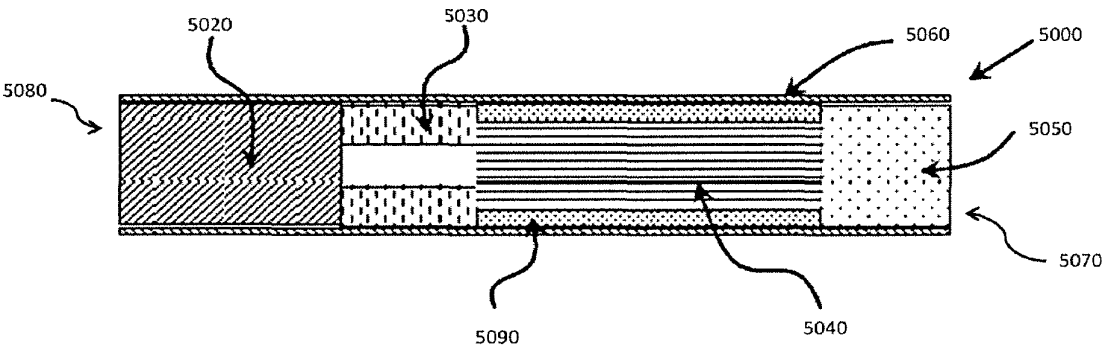


FIGURE 3

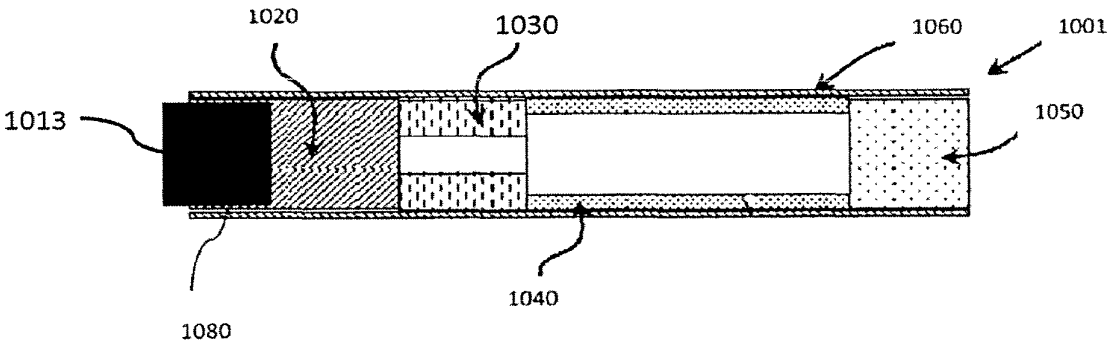


FIGURE 4

3/3

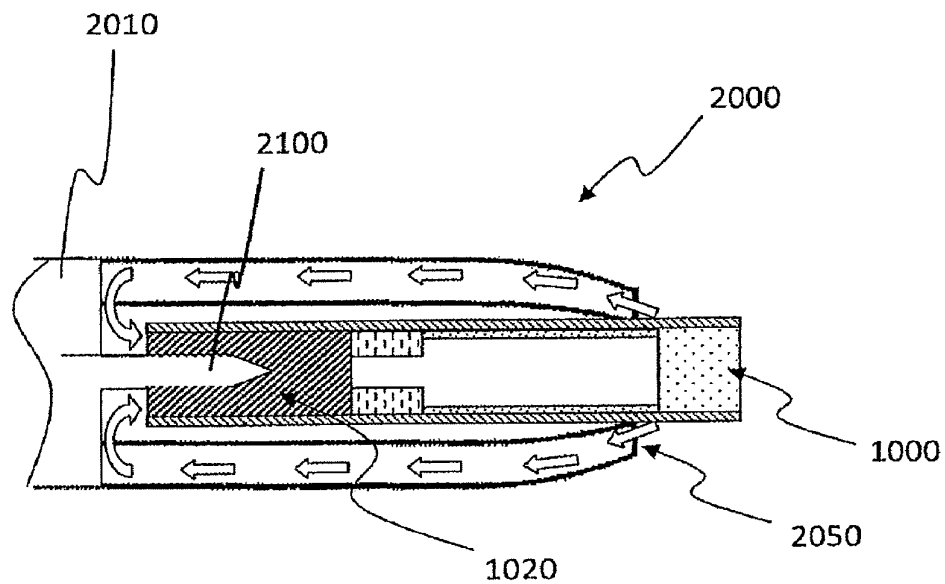


FIGURE 5

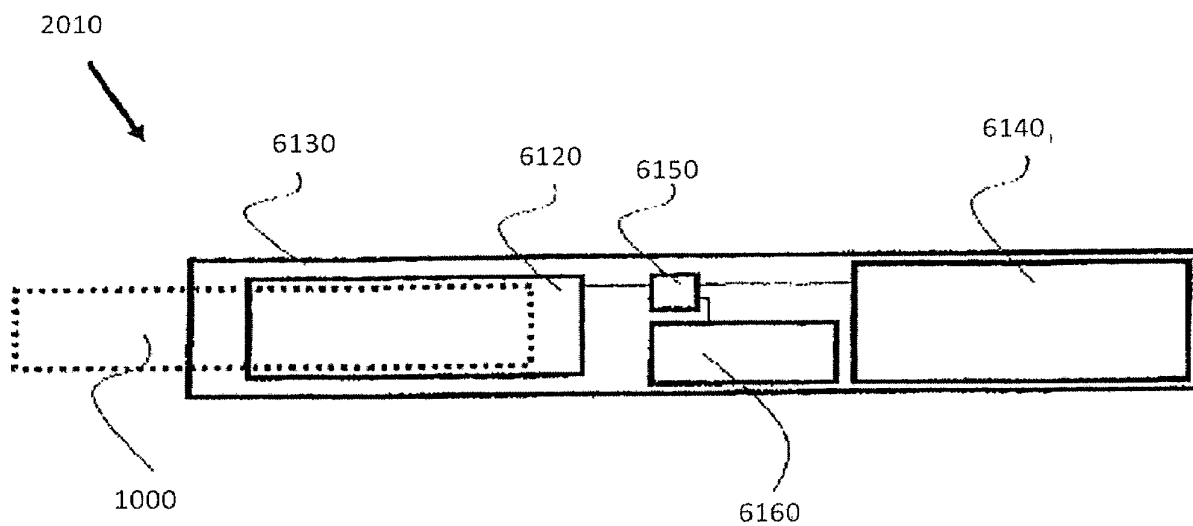


FIGURE 6

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/076650

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24F47/00

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/070288 A2 (PHILIP MORRIS PROD [CH]) 6 July 2006 (2006-07-06) the whole document -----	1-5,7, 10,12
A	US 2011/041861 A1 (SEBASTIAN ANDRIES DON [US] ET AL) 24 February 2011 (2011-02-24) the whole document -----	1-14
A	US 5 778 899 A (SAITO YUTAKA [JP] ET AL) 14 July 1998 (1998-07-14) the whole document -----	1-14
A	US 5 746 227 A (ROSE JED E [US] ET AL) 5 May 1998 (1998-05-05) the whole document -----	1-14



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

11 March 2015

Date of mailing of the international search report

18/03/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

MacCormick, Duncan

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/076650

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2006070288	A2	06-07-2006	US 2006283468 A1	21-12-2006
			US 2013074854 A1	28-03-2013
			US 2014345630 A1	27-11-2014
			WO 2006070288 A2	06-07-2006

US 2011041861	A1	24-02-2011	CN 102481021 A	30-05-2012
			EP 2470033 A1	04-07-2012
			JP 2013502232 A	24-01-2013
			US 2011041861 A1	24-02-2011
			US 2013233329 A1	12-09-2013
			WO 2011028372 A1	10-03-2011

US 5778899	A	14-07-1998	AT 174478 T	15-01-1999
			AT 200611 T	15-05-2001
			AU 669831 B2	20-06-1996
			AU 682921 B2	23-10-1997
			AU 1466795 A	15-08-1995
			AU 1466895 A	15-08-1995
			BG 62427 B1	30-11-1999
			BG 62428 B1	30-11-1999
			BG 100090 A	31-05-1996
			BG 100091 A	31-05-1996
			BR 9505831 A	12-03-1996
			BR 9505832 A	12-03-1996
			CA 2159118 A1	03-08-1995
			CA 2159119 A1	03-08-1995
			CN 1123000 A	22-05-1996
			CN 1123001 A	22-05-1996
			CZ 9502789 A3	13-03-1996
			CZ 9502790 A3	13-03-1996
			DE 69506628 D1	28-01-1999
			DE 69506628 T2	17-06-1999
			DE 69520708 D1	23-05-2001
			DE 69520708 T2	02-08-2001
			EP 0691083 A1	10-01-1996
			EP 0691084 A1	10-01-1996
			FI 954539 A	25-09-1995
			FI 954540 A	25-09-1995
			GR 3036163 T3	31-10-2001
			HK 1012529 A1	12-05-2000
			HK 1012530 A1	28-12-2001
			JP 3118462 B2	18-12-2000
			JP 3118463 B2	18-12-2000
			NO 953782 A	23-11-1995
			NO 953783 A	23-11-1995
			RU 2085091 C1	27-07-1997
			RU 2085092 C1	27-07-1997
			SG 43868 A1	14-11-1997
			SG 44831 A1	19-12-1997
			SK 133395 A3	01-10-1996
			SK 133495 A3	03-07-1996
			US 5778899 A	14-07-1998
			WO 9520329 A1	03-08-1995
			WO 9520330 A1	03-08-1995

US 5746227	A	05-05-1998	AT 266951 T	15-06-2004
			AU 693783 B2	09-07-1998
			AU 6171994 A	29-08-1994

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/076650

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		AU 6380498 A	18-06-1998
		CA 2154873 A1	18-08-1994
		DE 69433788 D1	24-06-2004
		DE 69433788 T2	23-06-2005
		DK 0683632 T3	12-07-2004
		EP 0683632 A1	29-11-1995
		EP 1470833 A1	27-10-2004
		ES 2220912 T3	16-12-2004
		NZ 262292 A	22-08-1997
		PT 683632 E	30-09-2004
		US 5441060 A	15-08-1995
		US 5687746 A	18-11-1997
		US 5746227 A	05-05-1998
		US 6595209 B1	22-07-2003
		WO 9417679 A1	18-08-1994

(10) International Publication Number
WO 2015/084544 A1(43) International Publication Date
11 June 2015 (11.06.2015)(51) International Patent Classification:
A24F 1/10 (2006.01)(21) International Application Number:
PCT/US2014/064690(22) International Filing Date:
7 November 2014 (07.11.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/912,507 5 December 2013 (05.12.2013) US(71) Applicant: **PLOOM, INC.** [US/US]; 660 Alabama Street,
2nd Floor, San Francisco, CA 94110 (US).(72) Inventors: **BOWEN, Adam**; 660 Alabama Street, 2nd
Floor, San Francisco, CA 94110 (US). **XING, Chenyue**;
660 Alabama Street, 2nd Floor, San Francisco, CA 94110
(US).(74) Agent: **STELZER, Andrew**; Wilson Sonsini Goodrich &
Rosati, 650 Page Mill Road, Palo Alto, CA 94304 (US).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).**Declarations under Rule 4.17:**

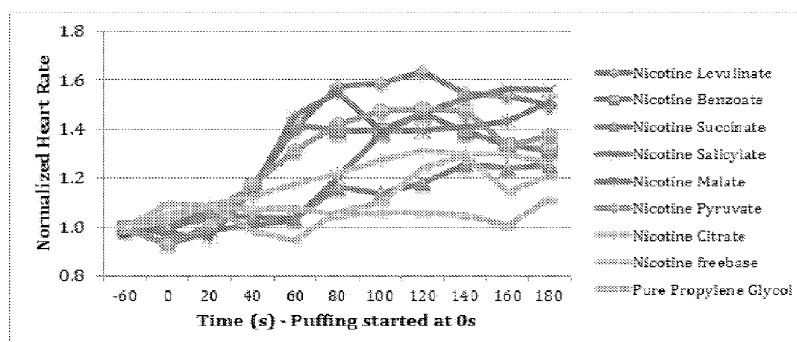
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))

(54) Title: NICOTINE LIQUID FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF

FIG. 1

(57) Abstract: A nicotine liquid formulation comprising nicotine, an acid, and a biologically acceptable liquid carrier, wherein heat-
ing an amount of said nicotine liquid formulation using low temperature electronic vaporization device, i.e. an electronic cigarette,
generates an inhalable aerosol, and wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least
about 90% of said nicotine in said amount is in said aerosol.

NICOTINE LIQUID FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF**CROSS REFERENCE**

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial No. 61/912,507, filed December 5, 2013, which is incorporated herein by reference in its entirety.

SUMMARY OF THE INVENTION

[0002] In some aspects, provided herein is a method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises said nicotine, an acid, and a biologically acceptable liquid carrier, wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0003] In some embodiments, said amount comprises about 4 μ L of said nicotine liquid formulation. In some embodiments, said amount comprises about 4.5 mg of said nicotine liquid formulation. In some embodiments, a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w). In some embodiments, a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1. In some embodiments, said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1. In some embodiments, said acid and said nicotine form a nicotine salt. In some embodiments, said nicotine is stabilized in said nicotine salt in said inhalable aerosol. In some embodiments of the methods described herein, said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt. In some embodiments of the methods described herein, one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user. In some embodiments of the methods described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid. In some embodiments of the methods described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, and salicylic acid. In some embodiments of the methods described herein, said acid is benzoic acid. In some embodiments of the methods described herein, said concentration is from about 2% (w/w) to about 6% (w/w). In some embodiments of the methods described herein, said concentration is about 5% (w/w). In some embodiments of the methods described herein, said biologically acceptable liquid carrier

comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin. In some embodiments of the methods described herein, said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin. In some embodiments of the methods described herein, said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C. In some embodiments of the methods described herein, said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C. In some embodiments of the methods described herein, said heater heats said amount of said nicotine liquid formulation to about 200 °C. In some embodiments of the methods described herein, said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid. In some embodiments of the methods described herein, said additional acid forms an additional nicotine salt. In some embodiments of the methods described herein, at least about 60% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the methods described herein, at least about 70% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the methods described herein, at least about 80% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the methods described herein, more than about 90% of said acid in said amount is in said aerosol.

[0004] In some aspects, provided herein is a method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises: said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w); an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0005] In some aspects, provided herein is a method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to a heater; the

heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0006] In some aspects, provided herein is a method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to a heater; the heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0007] In some aspects, provided herein is a method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to a heater; the heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said benzoic acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0008] In some aspects, provided herein is a cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising said nicotine, an acid, and a biologically acceptable liquid carrier, wherein using said electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0009] In some embodiments of the cartridges described herein, said amount comprises about 4 μ L of said nicotine liquid formulation. In some embodiments of the cartridges described herein, said amount comprises about 4.5 mg of said nicotine liquid formulation. In some

embodiments of the cartridges described herein, a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w). In some embodiments of the cartridges described herein, a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1. In some embodiments of the cartridges described herein, said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1. In some embodiments of the cartridges described herein, said acid and said nicotine form a nicotine salt. In some embodiments of the cartridges described herein, said nicotine is stabilized in said nicotine salt in said inhalable aerosol. In some embodiments of the cartridges described herein, said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt. In some embodiments of the cartridges described herein, one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user. In some embodiments of the cartridges described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid. In some embodiments of the cartridges described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, and salicylic acid. In some embodiments of the cartridges described herein, said acid is benzoic acid. In some embodiments of the cartridges described herein, said concentration is from about 2% (w/w) to about 6% (w/w). In some embodiments of the cartridges described herein, said concentration is about 5% (w/w). In some embodiments of the cartridges described herein, said biologically acceptable liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin. In some embodiments of the cartridges described herein, said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin. In some embodiments of the cartridges described herein, said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C. In some embodiments of the cartridges described herein, said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C. In some embodiments of the cartridges described herein, said heater heats said amount of said nicotine liquid formulation to about 200 °C. In some embodiments of the cartridges described herein, said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid. In some embodiments of the cartridges described herein, said additional acid forms an additional nicotine salt. In some embodiments of the cartridges described herein, at least about 60% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the cartridges described herein, at least about 70% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the cartridges described herein, at least about 80% to about 90% of said acid in said amount is in

said aerosol. In some embodiments of the cartridges described herein, more than about 90% of said acid in said amount is in said aerosol.

[0010] In some aspects, provided here is a cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising: said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w); an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using said electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0011] In some aspects, provided here is a cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising: said nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier wherein using said electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0012] In some aspects, provided here is a cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising: said nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using said electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0013] In some aspects, provided here is a cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment

comprising a nicotine formulation comprising: said nicotine at a concentration from about 2% (w/w) to about 6% (w/w); benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to a heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said benzoic acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0014] In some aspects, provided here is a formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising nicotine, an acid, and a biologically acceptable liquid carrier, wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0015] In some embodiments of the formulations described herein, said amount comprises about 4 μ L of said nicotine liquid formulation. In some embodiments of the formulations described herein, wherein said amount comprises about 4.5 mg of said nicotine liquid formulation. In some embodiments of the formulations described herein, a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w). In some embodiments of the formulations described herein, a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1. In some embodiments of the formulations described herein, said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1. In some embodiments of the formulations described herein, said acid and said nicotine form a nicotine salt. In some embodiments of the formulations described herein, wherein said nicotine is stabilized in said nicotine salt in said inhalable aerosol. In some embodiments of the formulations described herein, said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt. In some embodiments of the formulations described herein, one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user. In some embodiments of the formulations described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid. In some embodiments of the formulations described herein, said acid is selected from the group consisting of: benzoic acid, pyruvic acid, and salicylic acid. In some embodiments of the formulations described herein, said acid is benzoic acid. In some embodiments of the formulations described herein, said concentration is from about 2% (w/w) to about 6% (w/w). In some embodiments of the

formulations described herein, said concentration is about 5% (w/w). In some embodiments of the formulations described herein, said biologically acceptable liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin. In some embodiments of the formulations described herein, said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin. In some embodiments of the formulations described herein, said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C. In some embodiments of the formulations described herein, said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C. In some embodiments of the formulations described herein, said heater heats said amount of said nicotine liquid formulation to about 200 °C. In some embodiments of the formulations described herein, said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid. In some embodiments of the formulations described herein, said additional acid forms an additional nicotine salt. In some embodiments of the formulations described herein, at least about 60% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the formulations described herein, at least about 70% to about 90% of said acid in said amount is in said aerosol. In some embodiments of the formulations described herein, at least about 80% to about 90% of said acid in said amount is in said aerosol. In some embodiments, wherein more than about 90% of said acid in said amount is in said aerosol.

[0016] In some aspects, provided herein is a formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising: said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w); an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; and said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0017] In some aspects, provided herein is a formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; and said heater forming an aerosol by heating said amount of

said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0018] In some aspects, provided herein is a formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and a biologically acceptable liquid carrier wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; and said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

[0019] In some aspects, provided herein is a formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising: nicotine at a concentration from about 2% (w/w) to about 6% (w/w); benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and a biologically acceptable liquid carrier; wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; and said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

INCORPORATION BY REFERENCE

[0020] All publications, patents and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are used, and the accompanying drawings of which:

[0022] **Figure 1** illustrates a non-limiting example of results of heart rate data measured for six minutes from start of puffing. Y-axis is heart rate (bpm) and X-axis represent duration of the test (-60 to 180 seconds);

[0023] **Figure 2** illustrates results of heart rate data measured for ten minutes from start of puffing. Y-axis is heart rate (bpm) and X-axis represents duration of the test (0 to 10 minutes);

[0024] **Figure 3** illustrates a non-limiting example of calculated vapor pressures of various acids relative to nicotine;

[0025] **Figure 4** depicts a non-limiting example of low temperature electronic vaporization device, i.e. an electronic cigarette, having a fluid storage compartment comprising an embodiment nicotine liquid formulation described herein; and

[0026] **Figure 5** depicts a non-limiting example of low temperature electronic vaporization device, i.e. an electronic cigarette, cartomizer having a fluid storage compartment, a heater, and comprising an embodiment nicotine liquid formulation described herein.

[0027] **Figure 6** depicts a non-limiting example of pharmacokinetic profiles for four test articles in a blood plasma study.

[0028] **Figure 7** depicts a non-limiting example of $C_{\max}$ for four test articles in a blood plasma study.

[0029] **Figure 8** depicts a non-limiting example of $T_{\max}$ for four test articles in a blood plasma study.

[0030] **Figure 9** depicts a non-limiting example of the correlation between a molar ratio of benzoic acid to nicotine and a percent nicotine captured from at least a portion of an aerosol generated using low temperature electronic vaporization device, i.e. an electronic cigarette, and a nicotine liquid formulation.

[0031] **Figure 10** depicts a non-limiting example of a percent nicotine captured from at least a portion of an aerosol generated using low temperature electronic vaporization device, i.e. an electronic cigarette, and a nicotine liquid formulation.

[0032] **Figure 11** depicts a non-limiting example of the correlation between a molar ratio of acid functional groups to nicotine and a percent nicotine captured from at least a portion of an aerosol generated using low temperature electronic vaporization device, i.e. an electronic cigarette, and a nicotine liquid formulation.

DETAILED DESCRIPTION OF THE INVENTION

[0033] Nicotine is a chemical stimulant and increases heart rate and blood pressure when provided to an individual or animal. Nicotine transfer to an individual is associated with a feeling of physical and/or emotional satisfaction. Conflicting reports have been published regarding the transfer efficiency of free base nicotine in comparison to mono- or di-protonated nicotine salts. Studies on the transfer efficiency of free base nicotine and nicotine salts are complex and have yielded unpredictable results. Further, such transfer efficiency studies have been performed under extremely high temperature conditions, comparable to smoking; therefore, they offer scant guidance on the transfer efficiency of free base nicotine and nicotine salts under low-temperature vaporization conditions, for example low temperature vaporization

device, i.e. an electronic cigarette, conditions. Some reports have posited that nicotine free base should give rise to a greater satisfaction in a user than any corresponding nicotine salt.

[0034] It has been unexpectedly discovered herein that certain nicotine liquid formulations provide satisfaction in an individual superior to that of free base nicotine, and more comparable to the satisfaction in an individual smoking a traditional cigarette. The satisfaction effect is consistent with an efficient transfer of nicotine to the lungs, for example the alveoli of the lungs, of an individual and a rapid rise of nicotine absorption in the plasma as shown, in a non-limiting example, in Examples 8, 13 and 14, at least. It has also been unexpectedly discovered herein that certain nicotine liquid formulations provide greater satisfaction than other nicotine liquid formulations. Such effect has been shown in blood plasma levels of example nicotine liquid formulations herein, as a non-limiting example, in Examples 3 and 8, at least. These results demonstrate a rate of nicotine uptake in the blood is higher for nicotine liquid formulations, for example nicotine salt liquid formulations, than nicotine freebase formulations. Moreover, the studies depicted herein, demonstrate that the transfer efficiency of a nicotine liquid formulation, for example a nicotine salt, is dependent on the acid used in the formulation. As demonstrated in, at least, the non-limiting Example 13, certain acids used in the nicotine liquid formulation result in better transfer from the liquid formulation to the vapor and/or the aerosol. Therefore, described herein are nicotine liquid formulations, for example a nicotine salt liquid formulation, for use in low temperature electronic vaporization device, i.e. an electronic cigarette, or the like, that provide a general satisfaction effect consistent with an efficient transfer of nicotine to the lungs of an individual and a rapid rise of nicotine absorption in the plasma. Provided herein, therefore, are devices, nicotine liquid formulations comprising one or more nicotine salts, systems, cartomizers, kits and methods that are used to inhale an aerosol generated from a nicotine salt liquid formulation in a low temperature vaporization device, i.e. low temperature electronic vaporization device, i.e. an electronic cigarette, through the mouth or nose as described herein or as would be obvious to one of skill in the art upon reading the disclosure herein.

[0035] Consistent with these satisfaction effects, it has unexpectedly been found herein that there is a difference between the $C_{\max}$ (maximum concentration) and $T_{\max}$ (time at which the maximum concentration is measured) when measuring blood plasma nicotine levels of freebase nicotine liquid formulations inhaled using a low temperature vaporization device, i.e. electronic cigarette, as compared to the $C_{\max}$ and $T_{\max}$ (similarly measuring blood plasma nicotine levels) of a traditional cigarette. Also consistent with these satisfaction effects, it has unexpectedly been found herein that there is a difference between the $C_{\max}$ and $T_{\max}$ when measuring blood plasma nicotine levels of freebase nicotine liquid formulations inhaled using a low temperature

vaporization device, i.e. electronic cigarette, as compared to the $C_{\max}$ and $T_{\max}$ (similarly measuring blood plasma nicotine levels) of nicotine liquid formulations, for example nicotine salt liquid formulations, inhaled using a low temperature vaporization device, i.e. electronic cigarette. Additionally, it has unexpectedly been found that there is a difference between the rate of nicotine uptake in the plasma of users inhaling freebase nicotine liquid formulations using a low temperature vaporization device, i.e. electronic cigarette, as compared to the rate of nicotine uptake in the plasma of users inhaling smoke of a traditional cigarette. Furthermore, it has unexpectedly been found that there is a difference between the rate of nicotine uptake in the plasma of users inhaling freebase nicotine liquid formulations using a low temperature vaporization device, i.e. electronic cigarette, as compared to the rate of nicotine uptake in the plasma of users inhaling nicotine liquid formulations, for example a nicotine salt liquid formulations, using a low temperature vaporization device, i.e. electronic cigarette.

[0036] In some embodiments, inhalation of a vapor and/or an aerosol generated using a freebase nicotine composition in a low temperature vaporization device, i.e. an electronic cigarette, is not necessarily comparable in blood plasma levels ($C_{\max}$ and $T_{\max}$) to a traditional cigarette's nicotine delivery to blood when inhaled. Further, inhalation of a vapor and/or an aerosol generated using a freebase nicotine composition in a low temperature vaporization device, i.e. an electronic cigarette, is not necessarily comparable in blood plasma levels ($C_{\max}$ and $T_{\max}$) to inhalation of a vapor and/or an aerosol comprising nicotine generated from a nicotine liquid formulation, for example a nicotine salt liquid formulation. Further, inhalation of a vapor and/or an aerosol generated using a freebase nicotine composition in a low temperature vaporization device, i.e. an electronic cigarette, is not necessarily comparable in blood plasma levels when measuring the rate of nicotine uptake in the blood within the first 0-8 minutes to a traditional cigarette's nicotine delivery to blood when inhaled. Further, inhalation of a vapor and/or an aerosol generated using a freebase nicotine composition in a low temperature vaporization device, i.e. an electronic cigarette, is not necessarily comparable in blood plasma levels when measuring the rate of nicotine uptake in the blood within the first 0-8 minutes to inhalation of a vapor and/or an aerosol comprising nicotine generated from a nicotine liquid formulation, for example a nicotine salt liquid formulation.

[0037] Consistent with the observed differences in nicotine blood plasma levels when using freebase nicotine as a source of nicotine in a low temperature vaporization device, i.e. an electronic cigarette, in comparison to a nicotine liquid formulation, for example a nicotine salt liquid formulation, the transfer efficiency of the nicotine liquid formulation delivers more nicotine from the liquid formulation to the vapor and/or to the aerosol. As demonstrated, in a non-limiting Example 13 freebase nicotine as a source of nicotine in low temperature electronic

vaporization device, i.e. an electronic cigarette, results in less nicotine present in an aerosol as compared to using a nicotine liquid formulation, for example a nicotine salt liquid formulation, as a source of nicotine in low temperature electronic vaporization device, i.e. an electronic cigarette. Further, this is consistent with the observed differences in nicotine blood plasma levels when using freebase nicotine as a source of nicotine in a low temperature vaporization device, i.e. an electronic cigarette, compared to using a nicotine liquid formulation, for example a nicotine salt liquid formulation, wherein the higher transfer efficiency of the nicotine liquid formulation from the liquid to the vapor and/or the aerosol results in a higher rate of nicotine uptake in the blood. One explanation for this observation is that the aerosol comprising nicotine, for example liquid droplets of the aerosol, is more readily delivered to the user's lungs and/or alveoli therein resulting in more efficient uptake into the user's bloodstream. Moreover, the aerosol is delivered in particles sized to be delivered through the oral or nasal cavity and to a user's lungs, for example the alveoli of a user's lungs.

[0038] Compared to vaporized nicotine, aerosolized nicotine is more likely to travel to a user's lungs and be absorbed in alveoli. One reason that aerosolized nicotine has a greater chance of being absorbed in the lungs compared to vaporized nicotine is, for example, vaporized nicotine has a greater chance of being absorbed in mouth tissues and upper respiratory tract tissues of the user. Moreover, it is likely nicotine will absorb at a slower rate in the mouth and upper respiratory tract compared to nicotine absorbed in the lung tissue thus resulting in a less satisfying effect for a user. As shown in non-limiting Examples 8 and 13, at least, using a low temperature electronic vaporization device, i.e. an electronic cigarette, to deliver nicotine to a user, there is a direct correlation between the time to max concentration of nicotine in blood ($T_{\max}$) to the amount of aerosolized nicotine delivered to aerosol. For example, using a freebase nicotine liquid formulation results in a significant decrease in the amount of aerosolized nicotine compared to nicotine benzoate (1:1 nicotine:benzoic acid molar ratio) and nicotine malate (1:2 nicotine:malate molar ratio). Further, as shown in a non-limiting Example 8, the $T_{\max}$ is longer for freebase compared to nicotine benzoic acid and nicotine malate resulting from less aerosolized nicotine and thus less rapid uptake in the user's lungs.

[0039] In comparison to acids that do not degrade at room temperature and/or an operating temperature(s) of the device, acids that degrade at room temperature and/or an operating temperature of the device require a higher molar ratio of acid to nicotine to transfer the same molar amount of the acid from the liquid to the aerosol. As such, in some embodiments, twice the molar amount of acids that degrade at room temperature and/or an operating temperature(s) of the device compared to acids that do not degrade is required to generate an aerosol comprising the same molar amount of nicotine in the aerosol, in some embodiments in a non-gas

phase (e.g. liquid droplets) of the aerosol. As shown in a non-limiting Example 13, the correlation between the benzoic acid to nicotine molar ratio and the percent of acid captured demonstrates that more acid is the aerosol, in some embodiments in a non-gas phase of the aerosol, and as such, more nicotine is likely present the aerosol, in some embodiments in a non-gas phase of the aerosol. Further, malic acid is known to decompose at about 150 °C, which is below the temperature at which low temperature electronic vaporization device, i.e. an electronic cigarette, operates, and as shown in a non-limiting Example 13, less than 50% of the malic acid in the liquid formulation is recovered when using malic acid in the nicotine liquid formulation. This is significantly different than 90% of benzoic acid in the liquid formulation being recovered when using benzoic acid in the nicotine liquid formulation. The lower percent recovery of malic acid is likely due to degradation of malic acid. Therefore, as shown in Example 13, about twice the amount of malic acid compared to benzoic acid is needed to generate an aerosol comprising the same molar amount of acid in the aerosol, in some embodiments in a non-gas phase of the aerosol, and as such, twice the amount of malic acid is more nicotine is likely required to generate an aerosol comprising the same amount of nicotine the aerosol, in some embodiments in a non-gas phase of the aerosol. Moreover, the degradation products of malic acid are likely present in the aerosol, which may be result in a user having an unfavorable experience when using the device and a malic acid nicotine liquid formulation. In some embodiments, an unfavorable experience comprises a flavor, a nervous response, and/or an irritation of one or more of an oral cavity, an upper respiratory tract, and/or the lungs.

[0040] The presence of acid in the aerosol stabilizes and/or carries nicotine to a user's lungs. In some embodiments, the formulation comprises a 1:1 ratio of moles of acid functional groups to moles of nicotine such that nicotine is stabilized in the aerosol produced by low temperature electronic vaporization device, i.e. an electronic cigarette. In some embodiments, the formulation comprises a 1:1 ratio of moles of carboxylic acid functional group hydrogens to moles of nicotine such that nicotine is stabilized in the aerosol produced by low temperature electronic vaporization device, i.e. an electronic cigarette. As shown in Example 14, nicotine is aerosolized at a 1:1 ratio of moles of benzoic acid to moles of nicotine, and since benzoic acid comprises one carboxylic acid functional group, nicotine is aerosolized at a 1:1 ratio of moles of carboxylic acid functional groups to moles of nicotine. Further, as shown in Example 14, nicotine is aerosolized at a 0.5:1 ratio of moles of succinic acid to moles of nicotine, and since succinic acid comprises two carboxylic acid functional groups, nicotine is aerosolized at a 1:1 ratio of moles of carboxylic acid functional groups to moles of nicotine. As shown in Example 14, each nicotine molecule is associated with one carboxylic acid functional group and thus is

likely protonated by the acid. Moreover, this demonstrates nicotine is likely delivered to the lungs of the user in a protonated form in the aerosol.

[0041] Some reasons for not using acids in a nicotine liquid formulation are listed below. Other reasons for using certain acids in a nicotine liquid formulation are unrelated to the rate of nicotine uptake. In some embodiments, an acid that is corrosive or otherwise incompatible with the electronic vaporization device materials is not used in the nicotine liquid formulation. As a non-limiting example, sulfuric acid would corrode and/or react with device components making it inappropriate to be included in the nicotine liquid formulation. In some embodiments, an acid that is toxic to a user of the electronic vaporization device is not useful in the nicotine liquid formulation because it is not compatible for human consumption, ingestion, or inhalation. As a non-limiting example, sulfuric acid is an example of such an acid, which may be inappropriate for a user of low temperature electronic vaporization device, i.e. an electronic cigarette, device, depending on the embodiment of the composition. In some embodiments, an acid in the nicotine liquid formulation is that is bitter or otherwise bad-tasting to a user is not useful in the nicotine liquid formulation. A non-limiting example of such an acid is acetic acid or citric acid at a high concentration. In some embodiments, acids that oxidize at room temperature and/or at the operating temperature of the device are not included in the nicotine liquid formulation. A non-limiting example of such acids comprises sorbic acid and malic, which are unstable at the room temperature and/or the operating temperature of the device. Decomposition of acids at room or operating temperatures may indicate that the acid is inappropriate for use in the embodiment formulations. As a non-limiting example, citric acid decomposes at 175°C, and malic acid decomposes at 140°C, thus for a device operating at 200°C, these acids may not be appropriate. In some embodiments, acids that have poor solubility in the composition constituents are inappropriate for use in certain embodiments of the compositions herein. As a non-limiting example, nicotine bitartrate with a composition of nicotine and tartaric acid at a 1:2 molar ratio will not produce a solution at a concentration of 0.5%(w/w) nicotine or higher and 0.9%(w/w) tartaric acid or higher in propylene glycol (PG) or vegetable glycerin (VG) or any mixture of PG and VG at ambient conditions. As used herein, weight percentage (w/w) refers to the weight of the individual component over the weight of the total formulation.

[0042] In some embodiments, a nicotine liquid formulation, for example a nicotine salt liquid formulation, made using an acid having a Vapor Pressure between 20 – 300 mmHg @ 200 °C, or Vapor Pressure > 20 mmHg @ 200 °C, or a Vapor Pressure from 20 to 300 mmHg @ 200 °C, or a Vapor Pressure from 20 to 200 mmHg @ 200 °C, a Vapor Pressure between 20 and 300 mmHg @ 200 °C provide satisfaction comparable to a traditional cigarette or closer to a traditional cigarette (as compared to other nicotine salt formulations or as compared to nicotine

freebase formulations). For non-limiting example, acids that meet one or more criteria of the prior sentence comprise salicylic acid, sorbic acid, benzoic acid, lauric acid, and levulinic acid. In some embodiments, a nicotine liquid formulation, for example a nicotine salt liquid formulation, made using an acid that has a difference between boiling point and melting point of at least 50 °C, and a boiling point greater than 160 °C, and a melting point less than 160 °C provide satisfaction comparable to a traditional cigarette or closer to a traditional cigarette (as compared to other nicotine salt formulations or as compared to nicotine freebase formulations). For non-limiting example, acids that meet the criteria of the prior sentence comprise salicylic acid, sorbic acid, benzoic acid, pyruvic acid, lauric acid, and levulinic acid. In some embodiments, a nicotine liquid formulation, for example a nicotine salt liquid formulation, made using an acid that has a difference between boiling point and melting point of at least 50 °C, and a boiling point at most 40 °C less than operating temperature, and a melting point at least 40 °C lower than operating temperature provide satisfaction comparable to a traditional cigarette or closer to a traditional cigarette (as compared to other nicotine salt formulations or as compared to nicotine freebase formulations). In some embodiments, an operating temperature can be 100 °C to 300°C, or about 200°C, about 150°C to about 250°C, 180°C to 220°C, about 180°C to about 220°C, 185°C to 215°C, about 185°C to about 215°C, about 190°C to about 210°C, 190°C to 210°C, 195°C to 205°C, or about 195°C to about 205°C. For non-limiting example, acids that meet the aforementioned criteria comprise salicylic acid, sorbic acid, benzoic acid, pyruvic acid, lauric acid, and levulinic acid. In some embodiments, a combination of these criteria for preference of certain nicotine salt formulations are contemplated herein.

[0043] As used in this specification and the claims, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise.

[0044] As used in this specification and the claims, the term “vapor” refers to a gas or a gas phase of a material. As used in the specification and the claims, the term “aerosol” refers to a colloidal suspension of particles, for example liquid droplets, dispersed in air or gas.

[0045] The term “organic acid” as used herein, refers to an organic compound with acidic properties (e.g., by Brønsted-Lowry definition, or Lewis definition). A common organic acid is the carboxylic acids, whose acidity is associated with their carboxyl group –COOH. A dicarboxylic acid possesses two carboxylic acid groups. The relative acidity of an organic is measured by its pK_a value and one of skill in the art knows how to determine the acidity of an organic acid based on its given pK_a value. The term “keto acid” as used herein, refers to organic compounds that contain a carboxylic acid group and a ketone group. Common types of keto acids include alpha-keto acids, or 2-oxoacids, such as pyruvic acid or oxaloacetic acid, having the keto group adjacent to the carboxylic acid; beta-keto acids, or 3-oxoacids, such as

acetoacetic acid, having the ketone group at the second carbon from the carboxylic acid; gamma-keto acids, or 4-oxoacids, such as levulinic acid, having the ketone group at the third carbon from the carboxylic acid.

[0046] The term “electronic cigarette” or “low temperature vaporization device” as used herein, refers to an electronic inhaler that vaporizes a liquid solution into an aerosol mist, simulating the act of tobacco smoking. The liquid solution comprises a formulation comprising nicotine. There are many a low temperature vaporization device, i.e. an electronic cigarette, which do not resemble conventional cigarettes at all. The amount of nicotine contained can be chosen by the user via the inhalation. In general, low temperature electronic vaporization device, i.e. an electronic cigarette, contains three essential components: a plastic cartridge that serves as a mouthpiece and a reservoir for liquid, an "atomizer" that vaporizes the liquid, and a battery. Other embodiment a low temperature vaporization device, i.e. an electronic cigarette, include a combined atomizer and reservoir, called a “cartomizer” that may or may not be disposable, a mouthpiece that may be integrated with the cartomizer or not, and a battery.

[0047] As used in this specification and the claims, unless otherwise stated, the term “about” refers to variations of 1%, 2%, 3%, 4%, 5%, 10%, 15%, or 25%, depending on the embodiment.

[0048] Suitable carriers (e.g., a liquid solvent) for the nicotine salts described herein include a medium in which a nicotine salt is soluble at ambient conditions, such that the nicotine salt does not form a solid precipitate. Examples include, but are not limited to, glycerol, propylene glycol, trimethylene glycol, water, ethanol and the like, as well as combinations thereof. In some embodiments, the liquid carrier comprises from about 0% to about 100% of propylene glycol and from about 100% to about 0% of vegetable glycerin. In some embodiments, the liquid carrier comprises from about 10% to about 70% of propylene glycol and from about 90% to about 30% of vegetable glycerin. In some embodiments, the liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin. In some embodiments, the liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin.

[0049] The formulations described herein vary in nicotine concentration. In some formulations, the concentration of nicotine in the formulation is dilute. In some formulations, the nicotine concentration in the formulation is less dilute. In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 1% (w/w) to about 25% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 1% (w/w) to about 20% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 1% (w/w) to about 18% (w/w). In some embodiments the concentration of nicotine in the nicotine liquid formulation is from about 1% (w/w) to about

15% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 4% (w/w) to about 12% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 2% (w/w) to about 6% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is about 5% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is about 4% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is about 3% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is about 2% (w/w). In some embodiments the concentration of nicotine in the nicotine liquid formulation is about 1% (w/w). In some formulations the concentration of nicotine in the nicotine liquid formulation is from about 1% (w/w) to about 25% (w/w).

[0050] The formulations described herein vary in nicotine salt concentration. In some formulations, the concentration of nicotine salt in the nicotine liquid formulation is dilute. In some formulations, the nicotine concentration in the formulation is less dilute. In some formulations the concentration of nicotine salt in the nicotine liquid formulation is from about 1% (w/w) to about 25% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is from about 1% (w/w) to about 20% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is from about 1% (w/w) to about 18% (w/w). In some embodiments the concentration of nicotine salt in the nicotine liquid formulation is from about 1% (w/w) to about 15% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is from about 4% (w/w) to about 12% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is from about 2% (w/w) to about 6% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is about 5% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is about 4% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is about 3% (w/w). In some formulations the concentration of nicotine salt in the nicotine liquid formulation is about 2% (w/w).

[0051] In some embodiments the concentration of nicotine salt in the nicotine liquid formulation is about 1% (w/w). In some formulations, a less dilute concentration of one nicotine salt is used in conjunction with a more dilute concentration of a second nicotine salt. In some formulations, the concentration of nicotine in the first nicotine liquid formulation is from about 1% to about 20%, and is combined with a second nicotine liquid formulation having a concentration of nicotine from about 1% to about 20% or any range or concentration therein. In some formulations, the concentration of nicotine salt in the first nicotine liquid formulation is from about 1% to about 20%, and is combined with a second nicotine liquid formulation having

a concentration of nicotine from 1% to 20% or any range or concentration therein. In some formulations, the concentration of nicotine salt in the first nicotine liquid formulation is from about 1% to about 20%, and is combined with a second nicotine liquid formulation having a concentration of nicotine salt from 1% to 20% or any range or concentration therein. As used with respect to concentrations of nicotine in the nicotine liquid formulations, the term “about” refers to ranges of 0.05% (i.e. if the concentration is from about 2%, the range is 1.95%-2.05%), 0.1 (i.e. if the concentration is from about 2%, the range is 1.9%-2.1%), 0.25 (i.e. if the concentration is from about 2%, the range is 1.75%-2.25%), 0.5 (i.e. if the concentration is from about 2%, the range is 1.5%-2.5%), or 1 (i.e. if the concentration is from about 4%, the range is 3%-5%), depending on the embodiment.

[0052] In some embodiments, the formulation comprises an organic acid and/or inorganic acid. In some embodiments, suitable organic acids comprise carboxylic acids. In some embodiments, organic carboxylic acids disclosed herein are monocarboxylic acids, dicarboxylic acids (organic acid containing two carboxylic acid groups), and carboxylic acids containing an aromatic group such as benzoic acids, hydroxycarboxylic acids, heterocyclic carboxylic acids, terpenoid acids, and sugar acids; such as the pectic acids, amino acids, cycloaliphatic acids, aliphatic carboxylic acids, keto carboxylic acids, and the like. In some embodiments, suitable acids comprise formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, citric acid, lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, phenylacetic acid, benzoic acid, pyruvic acid, levulinic acid, tartaric acid, lactic acid, malonic acid, succinic acid, fumaric acid, gluconic acid, saccharic acid, salicylic acid, sorbic acid, malonic acid, malic acid, or a combination thereof. In some embodiments, a suitable acid comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid. In some embodiments, a suitable acid comprises one or more of benzoic acid, pyruvic acid, and salicylic acid. In some embodiments, a suitable acid comprises benzoic acid.

[0053] Nicotine salts are formed by the addition of a suitable acid, including organic or inorganic acids. In some embodiments, suitable organic acids comprise carboxylic acids. In some embodiments, organic carboxylic acids disclosed herein are monocarboxylic acids, dicarboxylic acids (organic acid containing two carboxylic acid groups), carboxylic acids containing an aromatic group such as benzoic acids, hydroxycarboxylic acids, heterocyclic carboxylic acids, terpenoid acids, sugar acids; such as the pectic acids, amino acids, cycloaliphatic acids, aliphatic carboxylic acids, keto carboxylic acids, and the like. In some embodiments, organic acids used herein are monocarboxylic acids. Nicotine salts are formed from the addition of a suitable acid to nicotine. In some embodiments, suitable acids comprise

formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, citric acid, lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, phenylacetic acid, benzoic acid, pyruvic acid, levulinic acid, tartaric acid, lactic acid, malonic acid, succinic acid, fumaric acid, gluconic acid, saccharic acid, salicylic acid, sorbic acid, maseonic acid, malic acid, or a combination thereof. In some embodiments, a suitable acid comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid. In some embodiments, a suitable acid comprises one or more of benzoic acid, pyruvic acid, and salicylic acid. In some embodiments, a suitable acid comprises benzoic acid.

[0054] In some embodiments, the formulation comprises various stoichiometric ratios and/or molar ratios of acid to nicotine, acidic functional groups to nicotine, and acidic functional group hydrogens to nicotine. In some embodiments, the stoichiometric ratios of the nicotine to acid (nicotine:acid) are 1:1, 1:2, 1:3, 1:4, 2:3, 2:5, 2:7, 3:4, 3:5, 3:7, 3:8, 3:10, 3:11, 4:5, 4:7, 4:9, 4:10, 4:11, 4:13, 4:14, 4:15, 5:6, 5:7, 5:8, 5:9, 5:11, 5:12, 5:13, 5:14, 5:16, 5:17, 5:18, or 5:19. In some formulations provided herein, the stoichiometric ratios of the nicotine to acid are 1:1, 1:2, 1:3, or 1:4. In some embodiments, the molar ratio of acid to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1. In some embodiments, the molar ratio of acidic functional groups to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1. In some embodiments, the molar ratio of acidic functional group hydrogens to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1. In some embodiments, the molar ratio of acid to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1. In some embodiments, the molar ratio of acidic functional groups to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1,

about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1. In some embodiments, the molar ratio of acidic functional group hydrogens to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.

[0055] Nicotine is an alkaloid molecule that comprises two basic nitrogens. It may occur in different states of protonation. For example, if no protonation exists, nicotine is referred to as the “free base.” If one nitrogen is protonated, then the nicotine is “mono-protonated.”

[0056] In some embodiments, nicotine liquid formulations are formed by adding a suitable acid to nicotine, stirring the neat mixture at ambient temperature or at elevated temperature, and then diluting the neat mixture with a carrier mixture, such as a mixture of propylene glycol and glycerin. In some embodiments, the suitable acid is completely dissolved by the nicotine prior to dilution. The suitable acid may not completely dissolved by the nicotine prior to dilution. The addition of the suitable acid to the nicotine to form a neat mixture may cause an exothermic reaction. The addition of the suitable acid to the nicotine to form a neat mixture may be conducted at 55 °C. The addition of the suitable acid to the nicotine to form a neat mixture may be conducted at 90 °C. The neat mixture may be cooled to ambient temperature prior to dilution. The dilution may be carried out at elevated temperature.

[0057] In some embodiments, nicotine liquid formulations are prepared by combining nicotine and a suitable acid in a carrier mixture, such as a mixture of propylene glycol and glycerin. The mixture of nicotine and a first carrier mixture is combined with a mixture of a suitable acid in a second carrier mixture. In some embodiments, the first and second carrier mixtures are identical in composition. In some embodiments, the first and second carrier mixtures are not identical in composition. In some embodiments, heating of nicotine/acid/carrier mixture is required to facilitate complete dissolution. In some embodiments, stirring of nicotine/acid/carrier mixture is sufficient to facilitate complete dissolution.

[0058] In some embodiments, nicotine liquid formulations are prepared and added to a solution of 3:7 ratio by weight of propylene glycol (PG)/vegetable glycerin (VG), and mixed thoroughly. While described herein as producing 10g of each of the formulations, all procedures noted *infra* are scalable. Other manners of formulation may also be employed from the formulations noted *infra*, without departing from the disclosure herein, and as would be known to one of skill in the art upon reading the disclosure herein.

[0059] In some embodiments, the acid included in the nicotine liquid formulation is determined by the vapor pressure of the acid. In some embodiments, the nicotine liquid formulation comprises an acid with a vapor pressure that is similar to the vapor pressure of free

base nicotine. In some embodiments, the nicotine liquid formulations are formed from an acid with a vapor pressure that is similar to the vapor pressure of free base nicotine at the heating temperature of the device. As a non-limiting example, Figure 3 illustrates this trend. Nicotine salts formed from nicotine and benzoic acid; nicotine and pyruvic acid; nicotine and salicylic acid; or nicotine and levulinic acid are salts that produce a satisfaction in an individual user consistent with efficient transfer of nicotine and a rapid rise in nicotine plasma levels. This pattern may be due to the mechanism of action during heating of the nicotine liquid formulation. The nicotine salt may disassociate at, or just below, the heating temperature of the device, resulting in a mixture of free base nicotine and the individual acid. At that point, if both the nicotine and acid have similar vapor pressures, they may aerosolize at the same time, giving rise to a transfer of both free base nicotine and the constituent acid to the user. In some embodiments, the nicotine liquid formulation, for example a nicotine salt liquid formulation, for generating an inhalable aerosol upon heating in low temperature electronic vaporization device, i.e. an electronic cigarette, may comprise a nicotine salt in a biologically acceptable liquid carrier; wherein the acid used to form said nicotine salt is characterized by a vapor pressure between 20 – 4000 mmHg at 200 °C. In some embodiments, the acid used to form the nicotine salt is characterized by vapor pressure between 20 – 2000 mmHg at 200 °C. In some embodiments, the acid used to form the nicotine salt is characterized by vapor pressure between 100 – 300 mmHg at 200 °C.

[0060] Unexpectedly, different nicotine liquid formulations produced varying degrees of satisfaction in an individual. In some embodiments, the extent of protonation of the nicotine salt effects satisfaction, such that more protonation was less satisfying as compared to less protonation. In some embodiments, nicotine, for example a nicotine salt, in the formulation, vapor, and/or aerosol is monoprotonated. In some embodiments, nicotine, for example a nicotine salt, in the formulation, vapor and/or aerosol is diprotonated. In some embodiments, nicotine, for example a nicotine salt, in the formulation, vapor and/or aerosol exists in more than one protonation state, e.g., an equilibrium of mono-protonated and di-protonated nicotine salts. In some embodiments, the extent of protonation of nicotine is dependent upon the stoichiometric ratio of nicotine:acid used in the salt formation reaction. In some embodiments, the extent of protonation of nicotine is dependent upon the solvent. In some embodiments, the extent of protonation of nicotine is unknown.

[0061] In some embodiments, monoprotonated nicotine salts produced a high degree of satisfaction in the user. For example, nicotine benzoate and nicotine salicylate are monoprotonated nicotine salts and produce a high degree of satisfaction in the user. The reason for this trend may be explained by a mechanism of action wherein the nicotine is first deprotonated

prior to transfer to the vapor with the constituent acid, then stabilized by the acid in the aerosol after re-protonation, and carried by the acid going down stream to the lungs of the user. In addition, the lack of satisfaction of free base nicotine indicates that a second factor may be important. A nicotine salt may be best performing when it is at its optimal extent of protonation, depending on the salt. For example, as depicted in a non-limiting Example 13, nicotine benzoate transfers the maximum amount of nicotine to the aerosol at a 1:1 ratio of benzoic acid to nicotine. A lower molar ratio results in less nicotine being transferred to the aerosol, and a higher than 1:1 molar ratio of benzoic acid to nicotine does results in the transfer of any additional nicotine to the aerosol. This may be explained as 1 mole of nicotine associates or interacts with 1 mole of benzoic acid to form a salt. When there is not enough benzoic acid to associate with all nicotine molecules, the free base nicotine left unprotonated in the formulation is vaporized thus reducing the satisfaction for the user.

[0062] In some embodiments, acids that degrade at room temperature or an operating temperature of a low temperature electronic vaporization device, i.e. a low temperature electronic cigarette, do not afford the same degree of satisfaction to a user. For example, twice the amount of malic acid, which degrades at the operating temperature of the low temperature electronic cigarette, compared to benzoic acid is required to transfer the same molar amount of the acid from the liquid to the aerosol. As such, in some embodiments, twice the molar amount of malic acid compared to benzoic acid is required to generate an aerosol comprising the same molar amount of nicotine in the aerosol, in some embodiments in a non-gas phase of the aerosol. Moreover, because malic acid comprises two carboxylic acid groups and benzoic acid comprises one, four times the amount of acidic functional groups are required when using malic acid compared to benzoic acid in the nicotine liquid formulation. Moreover, because malic acid comprises two carboxylic acid groups and benzoic acid comprises one, four times the amount of acidic functional group hydrogens are required when using malic acid compared to benzoic acid in the nicotine liquid formulation. In some embodiments, the one or more chemicals produced on degradation of the acid results in an unfavorable experience to the user. In some embodiments, an unfavorable experience comprises a flavor, a nervous response, and/or an irritation of one or more of an oral cavity, an upper respiratory tract, and/or the lungs.

[0063] In some embodiments, provided here are method, systems, devices, formulations, and kits for generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises said nicotine, an acid, and a biologically acceptable liquid carrier, wherein using the electronic cigarette comprises: providing an amount of said nicotine liquid formulation to said heater; said

heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol. In some embodiments, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least 95%, or at least about 99% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 99% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 95% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 90% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 80% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 70% of said acid in said amount is in said aerosol. In some embodiments, at least about 50% to about 60% of said acid in said amount is in said aerosol. In some embodiments, at least about 60% to about 99% of said acid in said amount is in said aerosol. In some embodiments, at least about 60% to about 95% of said acid in said amount is in said aerosol. In some embodiments, at least about 60% to about 90% of said acid in said amount is in said aerosol. In some embodiments, at least about 60% to about 80% of said acid in said amount is in said aerosol. In some embodiments, at least about 60% to about 70% of said acid in said amount is in said aerosol. In some embodiments, at least about 70% to about 99% of said acid in said amount is in said aerosol. In some embodiments, at least about 70% to about 95% of said acid in said amount is in said aerosol. In some embodiments, at least about 70% to about 90% of said acid in said amount is in said aerosol. In some embodiments, at least about 70% to about 80% of said acid in said amount is in said aerosol.

[0064] In some embodiments, the aerosol is delivered in particles sized to be delivered through the oral or nasal cavity and to a user's lungs, for example the alveoli of a user's lungs. In some embodiments, the aerosol generated using a nicotine liquid formulation, for example a nicotine salt liquid formulation, generated using a low temperature vaporization device, for example a low temperature electronic cigarette, is delivered in particles sized to be delivered through the oral or nasal cavity and to a user's lungs, for example the alveoli of a user's lung. In some embodiments, the rate of uptake in the user's lungs, for example alveoli in the user's lungs, is affected by aerosol particle size. In some embodiments the aerosol particles are sized from about 0.1 microns to about 5 microns, from about 0.1 microns to about 4.5 microns, from about 0.1 microns to about 4 microns, from about 0.1 microns to about 3.5 microns, from about 0.1 microns to about 3 microns, from about 0.1 microns to about 2.5 microns, from about 0.1 microns to about 2 microns, from about 0.1 microns to about 1.5 microns, from about 0.1 microns to about 1 microns, from about 0.1 microns to about 0.9 microns, from about 0.1 microns to about 0.8 microns, from about 0.1 microns to about 0.7 microns, from about 0.1

[illegible]

microns, from about 0.6 microns to about 1 microns, from about 0.6 microns to about 0.9 microns, from about 0.6 microns to about 0.8 microns, from about 0.6 microns to about 0.7 microns, from about 0.8 microns to about 5 microns, from about 0.8 microns to about 4.5 microns, from about 0.8 microns to about 4 microns, from about 0.8 microns to about 3.5 microns, from about 0.8 microns to about 3 microns, from about 0.8 microns to about 2.5 microns, from about 0.8 microns to about 2 microns, from about 0.8 microns to about 1.5 microns, from about 0.8 microns to about 1 microns, from about 0.8 microns to about 0.9 microns, from about 0.9 microns to about 5 microns, from about 0.9 microns to about 4.5 microns, from about 0.9 microns to about 4 microns, from about 0.9 microns to about 3.5 microns, from about 0.9 microns to about 3 microns, from about 0.9 microns to about 2.5 microns, from about 0.9 microns to about 2 microns, from about 0.9 microns to about 1.5 microns, from about 0.9 microns to about 1 microns, from about 1 microns to about 5 microns, from about 1 microns to about 4.5 microns, from about 1 microns to about 4 microns, from about 1 microns to about 3.5 microns, from about 1 microns to about 3 microns, from about 1 microns to about 2.5 microns, from about 1 microns to about 2 microns, from about 1 microns to about 1.5 microns

[0065] In some embodiments, an amount of nicotine liquid formulation provided to said heater comprises a volume or a mass. In some embodiments the amount is quantified “per puff.” In some embodiments the amount comprises a volume of about 1 μ L, about 2 μ L, about 3 μ L, about 4 μ L, about 5 μ L, about 6 μ L, about 7 μ L, about 8 μ L, about 9 μ L, about 10 μ L, about 15 μ L, about 20 μ L, about 25 μ L, about 30 μ L, about 35 μ L, about 40 μ L, about 45 μ L, about 50 μ L, about 60 μ L, about 70 μ L, about 80 μ L, about 90 μ L, about 100 μ L, or greater than about 100 μ L. In some embodiments the amount comprises a mass of about 1 mg, about 2 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, or greater than about 100 mg.

[0066] The flavor of the constituent acid used in the salt formation may be a consideration in choosing the acid. A suitable acid may have minimal or no toxicity to humans in the concentrations used. A suitable acid may be compatible with the electronic cigarette components it contacts or could contact at the concentrations used. That is, such acid does not degrade or otherwise react with the electronic cigarette components it contacts or could contact. The odor of the constituent acid used in the salt formation may be a consideration in choosing a suitable acid. The concentration of the nicotine salt in the carrier may affect the satisfaction in the individual user. In some embodiments, the flavor of the formulation is adjusted by changing

the acid. In some embodiments, the flavor of the formulation is adjusted by adding exogenous flavorants. In some embodiments, an unpleasant tasting or smelling acid is used in minimal quantities to mitigate such characteristics. In some embodiments, exogenous pleasant smelling or tasting acid is added to the formulation. Examples of salts which can provide flavor and aroma to the mainstream aerosol at certain levels include nicotine acetate, nicotine oxalate, nicotine malate, nicotine isovalerate, nicotine lactate, nicotine citrate, nicotine phenylacetate and nicotine myristate.

[0067] Nicotine liquid formulations may generate an inhalable aerosol upon heating in low temperature electronic vaporization device, i.e. an electronic cigarette. The amount of nicotine or nicotine salt aerosol inhaled may be user-determined. The user may, for example, modify the amount of nicotine or nicotine salt inhaled by adjusting his inhalation strength.

[0068] Formulations are described herein comprising two or more nicotine salts. In some embodiments, wherein a formulation comprises two or more nicotine salts, each individual nicotine salt is formed as described herein.

[0069] Nicotine liquid formulations, as used herein, refer to a single or mixture of nicotine salts with other suitable chemical components used for electronic cigarette, such as carriers, stabilizers, diluents, dispersing agents, suspending agents, thickening agents, and/or excipients. In certain embodiments, the nicotine liquid formulation is stirred at ambient conditions for 20 minutes. In certain embodiments, the nicotine liquid formulation is heated and stirred at 55C for 20 minutes. In certain embodiments, the nicotine liquid formulation is heated and stirred at 90C for 60 minutes. In certain embodiments, the formulation facilitates administration of nicotine to an organism (e.g., lung).

[0070] The nicotine of nicotine liquid formulations provided herein is either naturally occurring nicotine (e.g., from extract of nicotineous species such as tobacco), or synthetic nicotine. In some embodiments, the nicotine is (-)-nicotine, (+)-nicotine, or a mixture thereof. In some embodiments, the nicotine is employed in relatively pure form (e.g., greater than about 80% pure, 85% pure, 90% pure, 95% pure, or 99 % pure). In some embodiments, the nicotine for nicotine liquid formulation provided herein is "water clear" in appearance in order to avoid or minimize the formation of tarry residues during the subsequent salt formation steps.

[0071] Nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein, in some embodiments, have a nicotine concentration of about 0.5% (w/w) to about 20% (w/w), wherein the concentration is of nicotine weight to total solution weight, i.e. (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 20% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to

about 18% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 15% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 4% (w/w) to about 12% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 18% (w/w), about 3% (w/w) to about 15% (w/w), or about 4% (w/w) to about 12% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 10% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 5% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 4% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 3% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 2% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 0.5% (w/w) to about 1% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 10% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 5% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 4% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 3% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 1% (w/w) to about 2% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 2% (w/w) to about 10% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 2% (w/w) to about 5% (w/w). In certain embodiments, nicotine liquid formulations provided herein have a nicotine concentration of about 2% (w/w) to about 4% (w/w). Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, 1.1%, 1.2%, 1.3%, 1.4%, 1.5%, 1.6%, 1.7%, 1.8%, 1.9%, 2.0%, 2.1%, 2.2%, 2.3%, 2.4%, 2.5%, 2.6%, 2.7%, 2.8%, 2.9%, 3.0%, 3.1%, 3.2%, 3.3%, 3.4%, 3.5%, 3.6%, 3.7%, 3.8%, 3.9%, 4.0%, 4.5%, 5.0%, 5.5%, 6.0%, 6.5%, 7.0%, 7.5%, 8.0%, 8.5%, 9.0%, 9.5%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, or 20% (w/w), or more, including any increments therein. Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 5% (w/w). Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 4% (w/w). Certain embodiments provide a nicotine

liquid formulation having a nicotine concentration of about 3% (w/w). Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 2% (w/w).

Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 1% (w/w). Certain embodiments provide a nicotine liquid formulation having a nicotine concentration of about 0.5% (w/w).

[0072] Nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein, in some embodiments, have a nicotine concentration of about 0.5% (w/w), 1% (w/w), about 2% (w/w), about 3% (w/w), about 4% (w/w), about 5% (w/w), about 6% (w/w), about 7% (w/w), about 8% (w/w), about 9% (w/w), about 10% (w/w), about 11% (w/w), about 12% (w/w), about 13% (w/w), about 14% (w/w), about 15% (w/w), about 16% (w/w), about 17% (w/w), about 18% (w/w), about 19% (w/w), or about 20% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 0.5% (w/w) to about 20% (w/w), from about 0.5% (w/w) to about 18% (w/w), from about 0.5% (w/w) to about 15% (w/w), from about 0.5% (w/w) to about 12% (w/w), from about 0.5% (w/w) to about 10% (w/w), from about 0.5% (w/w) to about 8% (w/w), from about 0.5% (w/w) to about 7% (w/w), from about 0.5% (w/w) to about 6% (w/w), from about 0.5% (w/w) to about 5% (w/w), from about 0.5% (w/w) to about 4% (w/w), from about 0.5% (w/w) to about 3% (w/w), or from about 0.5% (w/w) to about 2% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 1% (w/w) to about 20% (w/w), from about 1% (w/w) to about 18% (w/w), from about 1% (w/w) to about 15% (w/w), from about 1% (w/w) to about 12% (w/w), from about 1% (w/w) to about 10% (w/w), from about 1% (w/w) to about 8% (w/w), from about 1% (w/w) to about 7% (w/w), from about 1% (w/w) to about 6% (w/w), from about 1% (w/w) to about 5% (w/w), from about 1% (w/w) to about 4% (w/w), from about 1% (w/w) to about 3% (w/w), or from about 1% (w/w) to about 2% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 2% (w/w) to about 20% (w/w), from about 2% (w/w) to about 18% (w/w), from about 2% (w/w) to about 15% (w/w), from about 2% (w/w) to about 12% (w/w), from about 2% (w/w) to about 10% (w/w), from about 2% (w/w) to about 8% (w/w), from about 2% (w/w) to about 7% (w/w), from about 2% (w/w) to about 6% (w/w), from about 2% (w/w) to about 5% (w/w), from about 2% (w/w) to about 4% (w/w), or from about 2% (w/w) to about 3% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 3% (w/w) to

about 20% (w/w), from about 3% (w/w) to about 18% (w/w), from about 3% (w/w) to about 15% (w/w), from about 3% (w/w) to about 12% (w/w), from about 3% (w/w) to about 10% (w/w), from about 3% (w/w) to about 8% (w/w), from about 3% (w/w) to about 7% (w/w), from about 3% (w/w) to about 6% (w/w), from about 3% (w/w) to about 5% (w/w), or from about 3% (w/w) to about 4% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 4% (w/w) to about 20% (w/w), from about 4% (w/w) to about 18% (w/w), from about 4% (w/w) to about 15% (w/w), from about 4% (w/w) to about 12% (w/w), from about 4% (w/w) to about 10% (w/w), from about 4% (w/w) to about 8% (w/w), from about 4% (w/w) to about 7% (w/w), from about 4% (w/w) to about 6% (w/w), or from about 4% (w/w) to about 5% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 5% (w/w) to about 20% (w/w), from about 5% (w/w) to about 18% (w/w), from about 5% (w/w) to about 15% (w/w), from about 5% (w/w) to about 12% (w/w), from about 5% (w/w) to about 10% (w/w), from about 5% (w/w) to about 8% (w/w), from about 5% (w/w) to about 7% (w/w), or from about 5% (w/w) to about 6% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 6% (w/w) to about 20% (w/w), from about 6% (w/w) to about 18% (w/w), from about 6% (w/w) to about 15% (w/w), from about 6% (w/w) to about 12% (w/w), from about 6% (w/w) to about 10% (w/w), from about 6% (w/w) to about 8% (w/w), or from about 6% (w/w) to about 7% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration from about 2% (w/w) to about 6% (w/w). In some embodiments, the nicotine liquid formulations used for a low temperature vaporization device, i.e. an electronic cigarette, described herein have a nicotine concentration of about 5% (w/w).

[0073] In some embodiments, the formulation further may comprise one or more flavorants. In some embodiments, the flavor of the formulation is adjusted by changing the acid. In some embodiments, the flavor of the formulation is adjusted by adding exogenous flavorants. In some embodiments, an unpleasant tasting or smelling acid is used in minimal quantities to mitigate such characteristics. In some embodiments, exogenous pleasant smelling or tasting acid is added to the formulation. Examples of salts which can provide flavor and aroma to the mainstream aerosol at certain levels include nicotine acetate, nicotine oxalate, nicotine malate, nicotine isovalerate, nicotine lactate, nicotine citrate, nicotine phenylacetate and nicotine myristate.

[0074] In some embodiments, the suitable acid for the nicotine liquid formulation has a vapor pressure >20 mmHg at 200 °C and is non-corrosive to the electronic cigarette or is non-toxic to humans. In some embodiments, the suitable acid for nicotine salt formation is selected from the group consisting of salicylic acid, formic acid, sorbic acid, acetic acid, benzoic acid, pyruvic acid, lauric acid, and levulinic acid.

[0075] In some embodiments, the suitable acid for the nicotine liquid formulation has a vapor pressure of about 20 to 200 mmHg at 200 °C and is non-corrosive to the electronic cigarette or is non-toxic to humans. In some embodiments, the suitable acid for nicotine salt formation is selected from the group consisting of salicylic acid, benzoic acid, lauric acid, and levulinic acid.

[0076] In some embodiments, the suitable acid for the nicotine liquid formulation has a melting point <160 °C, a boiling point >160 °C, at least a 50-degree difference between the melting point and the boiling point, and is non-corrosive to the electronic cigarette or is non-toxic to humans. In some embodiments, the suitable acid for nicotine salt formation has a melting point at least 40 degrees lower than the operating temperature of the electronic cigarette, a boiling point no more than 40 degrees lower than the operating temperature of the electronic cigarette, at least a 50-degree difference between the melting point and the boiling point, and is non-corrosive to the electronic cigarette or is non-toxic to humans; wherein the operating temperature is 200 °C. In some embodiments, the suitable acid for nicotine salt formation is selected from the group consisting of salicylic acid, sorbic acid, benzoic acid, pyruvic acid, lauric acid, and levulinic acid.

[0077] In some embodiments, the suitable acid for the nicotine liquid formulation does not decompose at the operating temperature of the electronic cigarette. In some embodiments, the suitable acid for nicotine salt formation does not oxidize at the operating temperature of the electronic cigarette. In some embodiments, the suitable acid for nicotine salt formation does not oxidize at room temperature. In some embodiments, the suitable acid for nicotine salt formation does not provide an unpleasant taste. In some embodiments, the suitable acid for nicotine salt formation has good solubility in a liquid formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette.

[0078] Provided herein is low temperature electronic vaporization device, i.e. an electronic cigarette, **2** having a fluid storage compartment **4** comprising an embodiment nicotine liquid formulation of any embodiment described herein within the fluid storage compartment described herein. An embodiment is shown in FIG. 4. The electronic cigarette **2** of FIG. 4 includes a mouth end **6**, and a charging end **8**. The mouth-end **6** includes a mouthpiece **10**. The charging end **8** may connect to a battery or a charger or both, wherein the battery is within a body of the electronic cigarette, and the charger is separate from the battery and couples to the

body or the battery to charge the battery. In some embodiments the electronic cigarette comprises a rechargeable battery within a body **14** of the electronic cigarette and the charge end **8** comprises a connection **12** for charging the rechargeable battery. In some embodiments, the electronic cigarette comprises a cartomizer that comprises the fluid storage compartment and an atomizer. In some embodiments, the atomizer comprises a heater. In some embodiments the fluid storage compartment **4** is separable from an atomizer. In some embodiments the fluid storage compartment **4** is replaceable as part of a replaceable cartridge. In some embodiments the fluid storage compartment **4** is refillable. In some embodiments, the mouthpiece **10** is replaceable.

[0079] Provided herein is a cartomizer **18** for low temperature electronic vaporization device, i.e. an electronic cigarette, **2** having a fluid storage compartment **4** comprising an embodiment nicotine liquid formulation of any embodiment described herein within the fluid storage compartment described herein. The cartomizer **18** embodiment of FIG. 5 includes a mouth end **6**, and a connection end **16**. The connection end **16** in the embodiment of FIG. 5 couples the cartomizer **14** to a body of low temperature electronic vaporization device, i.e. an electronic cigarette,, or to a battery of the electronic cigarette, or both. The mouth end **6** includes a mouthpiece **10**. In some embodiments, the cartomizer does not include a mouthpiece, and in such embodiments, the cartomizer can be coupled to a mouthpiece of low temperature electronic vaporization device, i.e. an electronic cigarette,, or the cartomizer can be coupled to a battery or body of low temperature electronic vaporization device, i.e. an electronic cigarette,, while the mouthpiece is also coupled to the battery or the body of the electronic cigarette. In some embodiments, the mouthpiece is integral with the body of the electronic cigarette. In some embodiments, including the embodiment of FIG. 5, the cartomizer **18** comprises the fluid storage compartment **4** and an atomizer (not shown). In some embodiments, the atomizer comprises a heater (not shown).

Examples

Example 1: Preparation of Nicotine liquid formulations

[0080] Various nicotine liquid formulations were prepared and added to a solution of 3:7 ratio by weight of propylene glycol (PG)/vegetable glycerin (VG), and mixed thoroughly. The examples shown below were used to make 10g of each of the formulations. All procedures are scalable.

[0081] For example, in order to make nicotine liquid formulations with a final nicotine free base equivalent concentration of 2% (w/w), the following procedures were applied to each individual formulation.

- Nicotine benzoate salt formulation: 0.15g benzoic acid was added to a beaker followed by adding 0.2g nicotine to the same beaker. The mixture was stirred at 55 °C for 20 minutes until benzoic acid was completely dissolved and an orange oily mixture was formed. The mixture was cooled down to ambient conditions. 9.65g PG/VG (3:7) solution was added to the orange nicotine benzoate salt and the mixture was stirred until a visually homogenous formulation solution was achieved.
- Nicotine benzoate salt formulation can also be made by adding 0.15g benzoic acid to a beaker followed by adding 0.2g nicotine and 9.65g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 55 °C for 20 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine citrate salt formulation was made by adding 0.47g citric acid to a beaker followed by adding 0.2g nicotine and 9.33g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine malate salt formulation was made by adding 0.33g Malic acid to a beaker followed by adding 0.2g nicotine and 9.47g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine succinate salt formulation was made by adding 0.29g succinic acid to a beaker followed by adding 0.2g nicotine and 9.51g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine salicylate salt formulation was made by adding 0.17g salicylic acid to a beaker followed by adding 0.2g nicotine and 9.63g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine salicylate salt formulation can also be made by adding 0.17g salicylic acid to a beaker followed by adding 0.2g nicotine to the same beaker. The mixture was stirred at 90 °C for 60 minutes until salicylic acid was completely dissolved and an orange oily mixture was formed. The mixture was either cooled to ambient conditions or kept at 90 °C when 9.63g PG/VG (3:7) solution was added. The mixture was then stirred at 90 °C until a visually homogenous formulation solution was achieved with no undissolved chemicals.
- Nicotine free base formulation was made by adding 0.2g nicotine to a beaker followed by adding 9.8g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at

ambient conditions for 10 minutes until a visually homogenous formulation solution was achieved.

[0082] For example, in order to make nicotine liquid formulations with a final nicotine free base equivalent concentration of 3% (w/w), the following procedures were applied to each individual formulation.

- Nicotine benzoate salt formulation: 0.23g benzoic acid was added to a beaker followed by adding 0.3g nicotine to the same beaker. The mixture was stirred at 55 °C for 20 minutes until benzoic acid was completely dissolved and an orange oily mixture was formed. The mixture was cooled down to ambient conditions. 9.47g PG/VG (3:7) solution was added to the orange nicotine benzoate salt and the blend was stirred until a visually homogenous formulation solution was achieved.

- Nicotine benzoate salt formulation can also be made by adding 0.23g benzoic acid to a beaker followed by adding 0.3g nicotine and 9.47g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 55 °C for 20 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine citrate salt formulation was made by adding 0.71g citric acid to a beaker followed by adding 0.3g nicotine and 8.99g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine malate salt formulation was made by adding 0.5g Malic acid to a beaker followed by adding 0.3g nicotine and 9.2g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine levulinate salt formulation was made by adding melted 0.64g levulinic acid to a beaker followed by adding 0.3g nicotine to the same beaker. The mixture was stirred at ambient conditions for 10 minutes. Exothermic reaction took place and oily product was produced. The mixture was allowed to cool down to ambient temperature and 9.06g PG/VG (3:7) solution was added to the same beaker. The mixture was then stirred at ambient conditions for 20 minutes until a visually homogenous formulation solution was achieved.

- Nicotine pyruvate salt formulation was made by adding 0.33g pyruvic acid to a beaker followed by adding 0.3g nicotine to the same beaker. The mixture was stirred at ambient conditions for 10 minutes. Exothermic reaction took place and oily product was produced. The mixture was allowed to cool down to ambient temperature and 9.37g PG/VG (3:7)

solution was added to the same beaker. The mixture was then stirred at ambient conditions for 20 minutes until a visually homogenous formulation solution was achieved.

- Nicotine succinate salt formulation was made by adding 0.44g succinic acid to a beaker followed by adding 0.3g nicotine and 9.26g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine salicylate salt formulation was made by adding 0.26g salicylic acid to a beaker followed by adding 0.3g nicotine and 9.44g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine salicylate salt formulation can also be made by adding 0.26g salicylic acid to a beaker followed by adding 0.3g nicotine to the same beaker. The mixture was stirred at 90 °C for 60 minutes until salicylic acid was completely dissolved and an orange oily mixture was formed. The mixture was either cooled to ambient conditions or kept at 90 °C when 9.44g PG/VG (3:7) solution was added. The blend was then stirred at 90C until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine free base formulation was made by adding 0.3g nicotine to a beaker followed by adding 9.7g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at ambient conditions for 10 minutes until a visually homogenous formulation solution was achieved.

[0083] For example, in order to make nicotine liquid formulations with a final nicotine free base equivalent concentration of 4% (w/w), the following procedures were applied to each individual formulation.

- Nicotine benzoate salt formulation: 0.3g benzoic acid was added to a beaker followed by adding 0.4g nicotine to the same beaker. The mixture was stirred at 55 °C for 20 minutes until benzoic acid was completely dissolved and an orange oily mixture was formed. The mixture was cooled down to ambient conditions. 9.7g PG/VG (3:7) solution was added to the orange nicotine benzoate salt and the blend was stirred until a visually homogenous formulation solution was achieved.

- Nicotine benzoate salt formulation can also be made by adding 0.3g benzoic acid to a beaker followed by adding 0.4g nicotine and 9.7g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 55 °C for 20 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

For example, in order to make nicotine liquid formulations with a final nicotine free base equivalent concentration of 5% (w/w), the following procedures were applied to each individual formulation.

- Nicotine benzoate salt formulation: 0.38g benzoic acid was added to a beaker followed by adding 0.5g nicotine to the same beaker. The mixture was stirred at 55 °C for 20 minutes until benzoic acid was completely dissolved and an orange oily mixture was formed. The mixture was cooled down to ambient conditions. 9.12g PG/VG (3:7) solution was added to the orange nicotine benzoate salt and the blend was stirred until a visually homogenous formulation solution was achieved.

- Nicotine benzoate salt formulation can also be made by adding 0.38g benzoic acid to a beaker followed by adding 0.5g nicotine and 9.12g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 55 °C for 20 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine malate salt formulation was made by adding 0.83g Malic acid to a beaker followed by adding 0.5g nicotine and 8.67g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine levulinate salt formulation was made by adding melted 1.07g levulinic acid to a beaker followed by adding 0.5g nicotine to the same beaker. The mixture was stirred at ambient conditions for 10 minutes. Exothermic reaction took place and oily product was produced. The mixture was allowed to cool down to ambient temperature and 8.43g PG/VG (3:7) solution was added to the same beaker. The mixture was then stirred at ambient conditions for 20 minutes until a visually homogenous formulation solution was achieved.

- Nicotine pyruvate salt formulation was made by adding 0.54g pyruvic acid to a beaker followed by adding 0.5g nicotine to the same beaker. The mixture was stirred at ambient conditions for 10 minutes. Exothermic reaction took place and oily product was produced. The mixture was allowed to cool down to ambient temperature and 8.96g PG/VG (3:7) solution was added to the same beaker. The mixture was then stirred at ambient conditions for 20 minutes until a visually homogenous formulation solution was achieved.

- Nicotine succinate salt formulation was made by adding 0.73g succinic acid to a beaker followed by adding 0.5g nicotine and 8.77g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine salicylate salt formulation was made by adding 0.43g salicylic acid to a beaker followed by adding 0.5g nicotine and 9.07g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at 90 °C for 60 minutes until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine salicylate salt formulation can also be made by adding 0.43g salicylic acid to a beaker followed by adding 0.5g nicotine to the same beaker. The mixture was stirred at 90 °C for 60 minutes until salicylic acid was completely dissolved and an orange oily mixture was formed. The mixture was either cooled to ambient conditions or kept at 90C when 9.07g PG/VG (3:7) solution was added. The blend was then stirred at 90 °C until a visually homogenous formulation solution was achieved with no undissolved chemicals.

- Nicotine free base formulation was made by adding 0.5g nicotine to a beaker followed by adding 9.5g PG/VG (3:7) solution to the same beaker. The mixture was then stirred at ambient conditions for 10 minutes until a visually homogenous formulation solution was achieved.

[0084] Various formulations comprising different nicotine salts can be prepared similarly, or different concentrations of the above-noted nicotine liquid formulations or other nicotine liquid formulations can be prepared as one of skill in the art would know to do upon reading the disclosure herein.

[0085] Various formulations comprising two or more nicotine salts can be prepared similarly in a solution of 3:7 ratio of propylene glycol (PG)/vegetable glycerin (VG). For example, 0.43g (2.5% w/w nicotine) of nicotine levulinate salt and 0.34 g (2.5% w/w nicotine) of nicotine acetate salt are added to 9.23g of PG/VG solution, to achieve a 5% w/w nicotine liquid formulation.

[0086] Also provided is another exemplary formulation. For example, 0.23g (1.33% w/w nicotine) of nicotine benzoate salt (molar ratio 1:1 nicotine/benzoic acid), 0.25g (1.33% w/w nicotine) of nicotine salicylate salt(molar ratio 1:1 nicotine/salicylic acid) and 0.28 g (1.34% w/w nicotine) of nicotine pyruvate salt (molar ratio 1:2 nicotine/pyruvic acid) are added to 9.25g of PG/VG solution, to achieve a 5% w/w nicotine liquid formulation.

Example 2: Heart rate study of nicotine solutions via electronic cigarette

[0087] Exemplary formulations of nicotine levulinate, nicotine benzoate, nicotine succinate, nicotine salicylate, nicotine malate, nicotine pyruvate, nicotine citrate, nicotine freebase, and a control of propylene glycol were prepared as noted in Example 1 in 3% w/w solutions and were administered in the same fashion by low temperature electronic vaporization device, i.e. an electronic cigarette, to the same human subject. About 0.5 mL of each solution was loaded into an "eRoll" cartridge atomizer (joyetech.com) to be used in the study. The atomizer was then

attached to an "eRoll" electronic cigarette (same manufacturer). The operating temperature was from about 150°C to about 250 °C, or from about 180°C to about 220 °C.

[0088] Heart rate measurements were taken for 6 minutes; from 1 minute before start of puffing, for 3 minutes during puffing, and continuing until 2 minutes after end of puffing. The test participant took 10 puffs over 3 minutes in each case. The base heart rate was the average heart rate over the first 1 minute before start of puffing. Heart rate after puffing started was averaged over 20-second intervals. Puffing (inhalation) occurred every 20 seconds for a total of 3 minutes. Normalized heart rate was defined as the ratio between individual heart rate data point and the base heart rate. Final results were presented as normalized heart rate, shown for the first 4 minutes in FIG. 1.

[0089] FIG. 1 summarizes results from heart rate measurements taken for a variety of nicotine liquid formulations. For ease of reference in reviewing FIG. 1, at the 180-second timepoint, from top to bottom (highest normalized heart rate to lowest normalized heart rate), the nicotine liquid formulations are as follows: nicotine salicylate formulation, nicotine malate formulation, nicotine levulinate formulation (nearly identical to nicotine malate formulation at 180 seconds, thus, as a second reference point: the nicotine malate formulation curve is lower than the nicotine levulinate formulation curve at the 160-second time point), nicotine pyruvate formulation, nicotine benzoate formulation, nicotine citrate formulation, nicotine succinate formulation, and nicotine free base formulation. The bottom curve (lowest normalized heart rate) at the 180-second timepoint is associated with the placebo (100% propylene glycol). The test formulations comprising a nicotine salt cause a faster and more significant rise in heart rate than the placebo. The test formulations comprising a nicotine salt also cause faster and more significant rise when compared with a nicotine freebase formulation with the same amount of nicotine by weight. In addition, the nicotine salts (e.g., nicotine benzoate and nicotine pyruvate) prepared from the acids having calculated vapor pressures between 20 - 200 mmHg at 200 °C (benzoic acid (171.66 mmHg), with the exception of pyruvic acid (having a boiling point of 165C), respectively) cause a faster rise in heart rate than the rest. The nicotine salts (e.g., nicotine levulinate, nicotine benzoate, and nicotine salicylate) prepared from the acids (benzoic acid, levulinic acid and salicylic acid, respectively) also cause a more significant heart rate increase. Thus, other suitable nicotine salts formed by the acids with the similar vapor pressure and/or similar boiling point may be used in accordance with the practice of the present invention. This experience of increased heart rate theoretically approaching or theoretically comparable to that of a traditional burned cigarette has not been demonstrated or identified in other electronic cigarette devices. Nor has it been demonstrated or identified in low temperature tobacco vaporization devices (electronic cigarettes) that do not burn the tobacco, even when a

nicotine salt was used (a solution of 20% (w/w) or more of nicotine salt) as an additive to the tobacco. Thus the results from this experiment are surprising and unexpected.

Example 3: Satisfaction Study of Nicotine salt Solution via electronic cigarette

[0090] In addition to the heart rate study shown in Example 2, nicotine liquid formulations (using 3% w/w nicotine liquid formulations as described in Example 1) were used to conduct a satisfaction study using 11 test participants. The test participant, low temperature electronic vaporization device, i.e. an electronic cigarette, and/or traditional cigarette user, was required to have no nicotine intake for at least 12 hours before the test. The participant took 10 puffs using low temperature electronic vaporization device, i.e. an electronic cigarette, (same as used in Example 2) over 3 minutes in each case, and then was asked to rate the level of physical and emotional satisfaction he or she felt on a scale of 0 - 10, with 0 being no physical or emotional satisfaction. Using the ratings provided for each formulation, the formulations were then ranked from 1-8 with 1 having the highest rating and 8 having the lowest rating. The rankings for each acid were then averaged over the 11 participants to generate average rankings in Table 1. Nicotine benzoate, nicotine pyruvate, nicotine salicylate, and nicotine levulinate all performed well, followed by nicotine malate, nicotine succinate, and nicotine citrate.

Table 1

% Nicotine (w/w)	Salt (molar ratio nicotine:acid)	Avg. Rank
3%	Benzoate (1:1)	2.9
3%	Pyruvate (1:2)	3.3
3%	Salicylate (1:1)	3.6
3%	Levulinate (1:3)	4.1
3%	Malate (1:2)	4.1
3%	Succinate (1:2)	4.4
3%	Citrate (1:2)	5.9
3%	Freebase (NA)	6.6

[0091] Based on the Satisfaction Study, the nicotine salts formulations with acids having vapor pressure ranges between >20 mmHg @ 200 °C, or 20-200 mmHg @ 200 °C, or 100 – 300 mmHg @ 200 °C provide more satisfaction than the rest (except the pyruvic acid which has

boiling point of 165 °C). For reference, it has been determined that salicylic acid has a vapor pressure of about 135.7 mmHg @ 200 °C, benzoic acid has a vapor pressure of about 171.7 mmHg @ 200 °C, and levulinic acid has a vapor pressure of about 149 mmHg @ 200 °C.

[0092] Further, based on the Satisfaction Study, nicotine liquid formulations, for example a nicotine salt liquid formulations, comprising acids that degrade at the operating temperature of the device (i.e. malic acid) were ranked low. However, nicotine liquid formulations, for example a nicotine salt liquid formulations, comprising acids that do not degrade at the operating temperature of the device (i.e. benzoic acid) were ranked high. Thus, acids prone to degradation at the operating temperature of the device are less favorable compared to acids not prone to degradation.

Example 4: Test formulation 1 (TF1):

[0093] A solution of nicotine levulinate in glycerol comprising nicotine salt used: 1.26g (12.6% w/w) of 1:3 nicotine levulinate 8.74g (87.4% w/w) of glycerol - Total weight 10.0g.

[0094] Neat nicotine levulinate was added to the glycerol, and mixed thoroughly. L-Nicotine has a molar mass of 162.2g, and levulinic acid molar mass is 116.1g. In a 1:3 molar ratio, the percentage of nicotine in nicotine levulinate by weight is given by: $162.2\text{g} / (162.2\text{g} + (3 \times 116.1\text{g})) = 31.8\%$ (w/w).

Example 5: Test formulation 2 (TF2):

[0095] A solution of free base nicotine in glycerol comprising 0.40g (4.00% w/w) of L-nicotine was dissolved in 9.60g (96.0% w/w) of glycerol and mixed thoroughly.

Example 6: Heart rate study of nicotine solutions via electronic cigarette:

[0096] Both formulations (TF1 and TF2) were administered in the same fashion by low temperature electronic vaporization device, i.e. an electronic cigarette, to the same human subject: about 0.6 mL of each solution was loaded into "eGo-C" cartridge atomizer (joyetech.com). The atomizer was then attached to an "eVic" electronic cigarette (same manufacturer). This model of electronic cigarette allows for adjustable voltage, and therefore wattage, through the atomizer. The operating temperature of the electronic cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C.

[0097] The atomizer in both cases has resistance 2.4ohms, and the electronic cigarette was set to 4.24V, resulting in 7.49W of power. ($P = V^2 / R$)

[0098] Heart rate was measured in a 30-second interval for ten minutes from start of puffing. Test participants took 10 puffs over 3 minutes in each case (solid line (2nd highest peak): cigarette, dark dotted line (highest peak): test formulation 1 (TF1 -nicotine liquid formulation), light dotted line: test formulation 2 (TF2 — nicotine liquid formulation). Comparison between cigarette, TF1, and TF2 is shown in FIG. 2.

[0099] It is clearly shown in FIG. 2 that the test formulation with nicotine levulinate (TF1) causes a faster rise in heart rate than just nicotine (TF2). Also, TF1 more closely resembles the rate of increase for a cigarette. Other salts were tried and also found to increase heart rate relative to a pure nicotine solution. Thus, other suitable nicotine salts that cause the similar effect may be used in accordance with the practice of the present invention. For example, other keto acids (alpha-keto acids, beta-keto acids, gamma-keto acids, and the like) such as pyruvic acid, oxaloacetic acid, acetoacetic acid, and the like. This experience of increased heart rate comparable to that of a traditional burned cigarette has not been demonstrated or identified in other electronic cigarette devices, nor has it been demonstrated or identified in low temperature tobacco vaporization devices that do not burn the tobacco, even when a nicotine salt was used (a solution of 20% (W/W) or more of nicotine salt) as an additive to the tobacco. Thus the results from this experiment are surprising and unexpected.

[0100] In addition, the data appears to correlate well with the previous findings shown in FIG. 2.

[0101] As previously noted in the Satisfaction Study, the nicotine salts formulations with acids having vapor pressures between 20 – 300 mmHg @ 200 °C provide more satisfaction than the rest, with the exception of the nicotine liquid formulation made with pyruvic acid, which has a boiling point of 165 °C, as noted in FIG. 3. Further, based on the Satisfaction Study, nicotine liquid formulations, for example a nicotine salt liquid formulations, comprising acids that degrade at the operating temperature of the device (i.e. malic acid) were ranked low, and nicotine liquid formulations, for example a nicotine salt liquid formulations, comprising acids that do not degrade at the operating temperature of the device (i.e. benzoic acid) were ranked high. Thus, acids prone to degradation at the operating temperature of the device are less favorable compared to acids not prone to degradation. Based on the findings herein, it was anticipated that these nicotine liquid formulations having one or more of the following properties:

- a Vapor Pressure between 20 – 300 mmHg @ 200 °C,
- a Vapor Pressure > 20 mmHg @ 200 °C,
- a difference between boiling point and melting point of at least 50 °C, and a boiling point greater than 160 °C, and a melting point less than 160 °C,
- a difference between boiling point and melting point of at least 50 °C, and a boiling point greater than 160 °C, and a melting point less than 160 °C,
- a difference between boiling point and melting point of at least 50 °C, and a boiling point at most 40 °C less than operating temperature, and a melting point at least 40 °C lower than operating temperature, and

- resistant to degradation at the operating temperature of the device.

[00102] $T_{\max}$ – Time to maximum blood concentration: Based on the results established herein, a user of low temperature electronic vaporization device, i.e. an electronic cigarette, comprising the nicotine liquid formulation will experience a comparable rate of physical and emotional satisfaction from using a formulation comprising a mixture of nicotine salts prepared with an appropriate acid at least 1.2X to 3X faster than using a formulation comprising a freebase nicotine. As illustrated in FIG. 1: Nicotine from a nicotine salts formulation appears to generate a heartbeat that is nearly 1.2 times that of a normal heart rate for an individual approximately 40 seconds after the commencement of puffing; whereas the nicotine from a nicotine freebase formulation appears to generate a heartbeat that is nearly 1.2 times that of a normal heart rate for an individual approximately 110 seconds after the commencement of puffing; a 2.75 X difference in time to achieve a comparable initial satisfaction level.

[00103] Again this would not be inconsistent with the data from FIG. 2, where the data illustrated that at approximately 120 seconds (2 minutes), the heart rate of test participants reached a maximum of 105 – 110 bpm with either a regular cigarette or a nicotine liquid formulation (TF1); whereas those same participants heart rates only reached a maximum of approximately 86 bpm at approximately 7 minutes with a nicotine freebase formulation (TF2); also a difference in effect of 1.2 times greater with nicotine salts (and regular cigarettes) versus freebase nicotine.

[00104] Further, when considering peak satisfaction levels (achieved at approximately 120 seconds from the initiation of puffing (time =0) and looking at the slope of the line for a normalized heart rate, the approximate slope of those nicotine liquid formulations that exceeded the freebase nicotine liquid formulation range between 0.0054 hr_n/sec and 0.0025 hr_n/sec. By comparison, the slope of the line for the freebase nicotine liquid formulation is about 0.002. This would suggest that the concentration of available nicotine will be delivered to the user at a rate that is between 1.25 and 2.7 times faster than a freebase formulation.

[00105] In another measure of performance; $C_{\max}$ – Maximum blood nicotine concentration; it is anticipated that similar rates of increase will be measured in blood nicotine concentration, as those illustrated above. That is, it was anticipated based on the findings herein, and unexpected based on the art known to date, that there would be comparable $C_{\max}$ between the common cigarette and certain nicotine liquid formulations, but with a lower $C_{\max}$ in a freebase nicotine solution.

[00106] Similarly, anticipated based on the findings herein, and unexpected based on the art known to date, that certain nicotine liquid formulations would have higher rate of nicotine

uptake levels in the blood at early time periods. Indeed, Example 8 presents data for two salt formulations consistent with these predictions which were made based on the findings and tests noted herein, and unexpected compared to the art available to date.

Example 7: Heart rate study of nicotine solutions via electronic cigarette

[00107] Exemplary formulations of nicotine levulinate, nicotine benzoate, nicotine succinate, nicotine salicylate, nicotine malate, nicotine pyruvate, nicotine citrate, nicotine sorbate, nicotine laurate, nicotine freebase, and a control of propylene glycol are prepared as noted in Example 1 and are administered in the same fashion by low temperature electronic vaporization device, i.e. an electronic cigarette, to the same human subject. About 0.5 mL of each solution is loaded into an "eRoll" cartridge atomizer (joyetech.com) to be used in the study. The atomizer is then attached to an "eRoll" electronic cigarette (same manufacturer). The operating temperature of the electronic cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C.

[00108] Heart rate measurements are taken for 6 minutes; from 1 minute before start of puffing, for 3 minutes during puffing, and continuing until 2 minutes after end of puffing. The test participant takes 10 puffs over 3 minutes in each case. The base heart rate is the average heart rate over the first 1 minute before start of puffing. Heart rate after puffing started is averaged over 20-second intervals. Normalized heart rate is defined as the ratio between individual heart rate data point and the base heart rate. Final results are presented as normalized heart rate.

Example 8: Blood Plasma testing

[00109] Blood plasma testing was conducted on 24 subjects (n = 24). Four test articles were used in this study: one reference cigarette and three nicotine liquid formulations used in low temperature electronic vaporization device, i.e. an electronic cigarette, having an operating temperature of the electronic cigarette from about 150°C to about 250 °C, or from about 180°C to about 220 °C. The reference cigarette was Pall Mall (New Zealand). Three nicotine liquid formulations were tested in the electronic cigarette: 2% free base (w/w based on nicotine), 2% benzoate (w/w based on nicotine, 1:1 molar ratio of nicotine to benzoic acid), and 2% malate (w/w based on nicotine, 1:2 molar ratio of nicotine to malic acid). The three nicotine liquid formulations were liquid formulations prepared as described in Example 1.

[00110] The concentration of nicotine in each of the formulations was confirmed using UV spectrophotometer (Cary 60, manufactured by Agilent). The sample solutions for UV analysis were made by dissolving 20mg of each of the formulations in 20mL 0.3% HCl in water. The sample solutions were then scanned in UV spectrophotometer and the characteristic nicotine peak at 259nm was used to quantify nicotine in the sample against a standard solution of 19.8 µg/mL nicotine in the same diluent. The standard solution was prepared by first dissolving

19.8mg nicotine in 10mL 0.3% HCl in water followed by a 1:100 dilution with 0.3% HCl in water. Nicotine concentrations reported for all formulations were within the range of 95%-105% of the claimed concentrations

[00111] All subjects were able to consume 30-55 mg of the liquid formulation of each tested blend using the electronic cigarette.

[00112] Literature results: C. Bullen et al, Tobacco Control 2010, 19:98-103

Cigarette (5min adlib, n=9): $T_{max} = 14.3$ (8.8-19.9), $C_{max} = 13.4$ (6.5-20.3)

1.4% E-cig (5min adlib, n=8): $T_{max} = 19.6$ (4.9-34.2), $C_{max} = 1.3$ (0.0-2.6)

Nicorette Inhalator (20mg/20min, n=10): $T_{max} = 32.0$ (18.7-45.3), $C_{max} = 2.1$ (1.0-3.1)

[00113] Estimated C_{max} of 2% nicotine blends:

$C_{max} = \text{Mass consumed} * \text{Strength} * \text{Bioavailability} / (\text{Vol of Distribution} * \text{Body Weight}) = 40\text{mg} * 2\% * 80\% / (2.6\text{L/kg} * 75\text{kg}) = 3.3 \text{ ng/mL}$

[00114] Estimated C_{max} of 4% nicotine blends:

$C_{max} = \text{Mass consumed} * \text{Strength} * \text{Bioavailability} / (\text{Vol of Distribution} * \text{Body Weight}) = 40\text{mg} * 4\% * 80\% / (2.6\text{L/kg} * 75\text{kg}) = 6.6 \text{ ng/mL}$

[00115] Pharmacokinetic profiles of the blood plasma testing are shown in FIG. 6; showing blood nicotine concentrations (ng/mL) over time after the first puff (inhalation) of the aerosol from the electronic cigarette or the smoke of the reference cigarette. Ten puffs were taken at 30 sec intervals starting at time =0 and continuing for 4.5 minutes. It is likely based on the data shown in FIG. 6 and in other studies herein that the freebase formulation is statistically different from salt formulations and/or the reference cigarette with respect to C_{max} , since it appears lower than others tested at several time points. Moreover, one of skill in the art, upon review of the disclosure herein could properly power a test to determine actual statistically-based differences between one or more formulations and the cigarette, or between the formulations themselves in low temperature electronic vaporization device, i.e. an electronic cigarette. For ease of reference Table 2 presents the amount of nicotine detected (as an average of all users) for each formulation and the reference cigarette, presented in ng/mL, along with C_{max} and T_{max} . Data from these tables, along with the raw data therefore, was used to generate FIG. 6, 7, and 8.

Table 2

Time	Pall Mall	2% Freebase	2% Benzoate	2% Malate
-2	0.07	-0.14	0.02	0.10
0	-0.03	0.14	-0.03	-0.15
1.5	4.54	0.22	1.43	1.91
3	17.12	1.50	5.77	5.18

5	24.85	2.70	7.35	7.65
7.5	16.36	2.60	4.73	4.79
10	13.99	2.87	3.90	3.71
12.5	12.80	2.79	3.11	3.10
15	11.70	2.30	2.79	2.64
30	7.65	1.14	1.64	1.06
60	4.47	0.04	0.37	0.06
$T_{\max}$ (min)	6.15	9.48	8.09	5.98
$C_{\max}$ (ng/mL)	29.37	4.56	9.27	8.75

[00116] Comparison of $C_{\max}$ and $T_{\max}$ of the three nicotine liquid formulations and reference cigarette are shown in FIG. 7. Due to the time limit of the wash-period, baseline blood nicotine concentration (at $t=-2$ and $t=0$ min) was higher for samples consumed at a later time on the test day. The data in FIGS. 6-7 show corrected blood nicotine concentration values (i.e. apparent blood nicotine concentration at each time point minus baseline nicotine concentration of the same sample). FIG. 8 depicts $T_{\max}$ data calculated using the corrected blood nicotine concentration. The reference cigarette, nicotine liquid formulation comprising nicotine benzoate, and nicotine liquid formulation comprising nicotine malate all exhibited a higher $C_{\max}$ and lower $T_{\max}$ than the nicotine liquid formulation comprising freebase nicotine. The superior performance of the nicotine liquid formulations comprising nicotine benzoate and nicotine malate compared to freebase nicotine is likely due to the superior transfer efficiency of the nicotine salt from the liquid to the aerosol compared to freebase nicotine, which allows nicotine to be delivered more efficiently to the user's lungs and/or alveoli of the user's lungs.

[00117] The nicotine liquid formulation contents and properties of the acids tested provide a plausible explanation as to how the blood plasma testing data corroborate the lower ranking of malic acid compared to benzoic acid as described in Example 1. In the blood plasma experiments the nicotine malate formulation comprised a 1:2 molar ratio of nicotine to malic acid and the nicotine benzoate formulation comprised a 1:1 molar ratio of nicotine to benzoic acid. As explained below, extra malic acid is needed to aerosolize nicotine because malic acid degrades at the operating temperature of the electronic cigarette. Thus, it is probable that the aerosol generated using malic acid comprises degradation products, which could result in an unfavorable experience for a user thus resulting in a lower ranking. For example, an unfavorable experience comprises a flavor, a nervous response, and/or an irritation of one or more of an oral cavity, an upper respiratory tract, and/or the lungs.

Example 9: Blood Plasma testing

[00118] Blood plasma testing is conducted on 24 subjects (n = 24). Eight test articles are used in this study: one reference cigarette and seven blends delivered to a user in low temperature electronic vaporization device, i.e. an electronic cigarette, as an aerosol. The operating temperature of the electronic cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C. The reference cigarette is Pall Mall (New Zealand). Seven blends are tested: 2% free base, 2% benzoate, 4% benzoate, 2% citrate, 2% malate, 2% salicylate, and 2% succinate. The seven blends are liquid formulations prepared according to protocols similar to that described *infra* and in Example 1.

[00119] All subjects are to consume 30-55 mg of the liquid formulation of each tested blend. Ten puffs are to be taken at 30 sec intervals starting at time =0 and continuing for 4.5 minutes. Blood plasma testing is to occur for at least 60 minutes from the first puff (t=0) Pharmacokinetic data (e.g., C_{max}, T_{max}, AUC) for nicotine in the plasma of users are obtained at various time periods during those 60 minutes, along with rates of nicotine absorption within the first 90 seconds for each test article.

Example 10: Blood Plasma testing

[00120] Blood plasma testing is conducted on twenty-four subjects (n = 24). Eleven test articles are used in this study: one reference cigarette and ten blends delivered to a user in low temperature electronic vaporization device, i.e. an electronic cigarette, as an aerosol. The reference cigarette is Pall Mall (New Zealand). The operating temperature of the electronic cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C. Ten blends are tested: 2% free base, 2% benzoate, 2% sorbate, 2% pyruvate, 2% laurate, 2% levulinate, 2% citrate, 2% malate, 2% salicylate, and 2% succinate. The ten blends are liquid formulations prepared according to protocols similar to that described *infra* and in Example 1.

[00121] All subjects are to consume 30-55 mg of the liquid formulation of each tested blend. Ten puffs are to be taken at 30 sec intervals starting at time =0 and continuing for 4.5 minutes. Blood plasma testing is to occur for at least 60 minutes from the first puff (t=0) . Pharmacokinetic data (e.g., C_{max}, T_{max}, AUC) for nicotine in the plasma of users are obtained at various time periods during those 60 minutes, along with rates of nicotine absorption within the first 90 seconds for each test article.

Example 11: Blood Plasma testing

[00122] Blood plasma testing is conducted on twenty-four subjects (n = 24). Twenty-one test articles are used in this study: one reference cigarette and twenty blends delivered to a user in low temperature electronic vaporization device, i.e. an electronic cigarette, as an aerosol. The reference cigarette is Pall Mall (New Zealand). The operating temperature of the electronic

cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C. Twenty blends are tested: 2% free base, 4% free base, 2% benzoate, 4% benzoate, 2% sorbate, 4% sorbate, 2% pyruvate, 4% pyruvate, 2% laurate, 4% laurate, 2% levulinate, 4% levulinate, 2% citrate, 4% citrate, 2% malate, 4% malate, 2% salicylate, 4% salicylate, 2% succinate, and 4% succinate. The twenty blends are liquid formulations prepared according to protocols similar to that described *infra* and in Example 1.

[00123] All subjects are to consume 30-55 mg of the liquid formulation of each tested blend. Ten puffs are to be taken at 30 sec intervals starting at time =0 and continuing for 4.5 minutes. Blood plasma testing is to occur for at least 60 minutes from the first puff (t=0) .

Pharmacokinetic data (e.g., C_{max}, T_{max}, AUC) for nicotine in the plasma of users are obtained at various time periods during those 60 minutes, along with rates of nicotine absorption within the first 90 seconds for each test article.

Example 12: Blood Plasma testing

[00124] Blood plasma testing is conducted on twenty-four subjects (n = 24). Twenty-one test articles are used in this study: one reference cigarette and twenty blends delivered to a user in low temperature electronic vaporization device, i.e. an electronic cigarette, as an aerosol. The reference cigarette is Pall Mall (New Zealand). The operating temperature of the electronic cigarette is from about 150°C to about 250 °C, or from about 180°C to about 220 °C. Twenty blends are tested: 2% free base, 1% free base, 2% benzoate, 1% benzoate, 2% sorbate, 1% sorbate, 2% pyruvate, 1% pyruvate, 2% laurate, 1% laurate, 2% levulinate, 1% levulinate, 2% citrate, 1% citrate, 2% malate, 1% malate, 2% salicylate, 1% salicylate, 2% succinate, and 1% succinate. The twenty blends are liquid formulations prepared according to protocols similar to that described *infra* and in Example 1.

[00125] All subjects are to consume 30-55 mg of the liquid formulation of each tested blend. Ten puffs are to be taken at 30 sec intervals starting at time =0 and continuing for 4.5 minutes. Blood plasma testing is to occur for at least 60 minutes from the first puff (t=0) .

Pharmacokinetic data (e.g., C_{max}, T_{max}, AUC) for nicotine in the plasma of users are obtained at various time periods during those 60 minutes, along with rates of nicotine absorption within the first 90 seconds for each test article.

Example 13: Aerosolized Nicotine Salt Testing

[00126] The experimental system comprised a glass bubbler (bubbler-1), a Cambridge filter pad, and 2 glass bubblers (trap-1 and trap-2, connected in sequence) to trap any volatiles that pass through the filter pad. Low temperature electronic vaporization device, i.e. an electronic cigarette, was connected to the inlet of bubbler 1, and was activated by a smoking machine connected to the outlet of trap 2 under designed puffing regime. The puffing regime comprised:

Number of puffs per sample=30, puff size=60 cc, puff duration=4s. The trap solvent comprised 0.3% HCl in water. The nicotine liquid formulations tested were: freebase nicotine, nicotine benzoate at molar ratios of nicotine to acid of 1:0.4, 1:0.7, 1:1, and 1:1.5, and nicotine malate at molar ratios of nicotine to acid of 1:0.5 and 1:2. The formulations were generated using the procedures described in Example 1. In the experimental system gaseous (i.e. vapor) analytes were captured by the bubblers.

[00127] The procedure comprised:

- weighing the following parts prior to the start of puffing: the electronic cigarette filled with nicotine liquid formulation, the bubbler-1 filled with 35mL trap solvent, a clean filter pad and pad holder, the trap-1 filled with 20mL trap solvent, and trap-2 filled with 20mL trap solvent;
- connecting in the following sequence: the electronic cigarette, bubbler-1, the filter pad, trap-1, trap-2, and the smoking machine;
- smoking was conducted under the aforementioned puffing regime. A clean air puff of the same puff size and duration was done after each smoking puff;
- weighing all parts after the end of the puffing regime. The inlet tubing of bubbler-1 was assayed with 10mL of trap solvent in aliquots of 1mL. The total solvent amount in bubbler-1 after puffing was calculated with the correction of water loss from 60 puffs. The filter pad was cut in half and each half was extracted in 20mL trap solvent for 2 hours. The pad extract was filtered through 0.2µm Nylon syringe filter. The front half of the pad holder was assayed with 5mL trap solvent. The back half of the pad holder was assayed with 3mL trap solvent;
- analyzing solutions by UV-Vis spectroscopy. The absorbance at 259nm was used to calculate the nicotine concentration. The absorbance at 230nm was used to calculate the benzoic acid concentration. Malic acid was quantified using Malic acid UV test kit from NZYTech Inc.

Results and Discussions

Analyte recovery

[00128] The total recovered amount of each analyte (nicotine, benzoic acid, and malic acid) was calculated as the sum of the assayed amount from all parts. No analyte was detected in trap-1 or trap-2. The percent recovery was calculated by dividing the total recovered amount by the theoretical amount generated by the electronic cigarette. Table 3 shows the percent recovery of nicotine in nicotine freebase liquid formulations, nicotine benzoate liquid formulations, and

nicotine malate liquid formulations. Table 3 also shows the percent recovery of benzoic acid in nicotine benzoate liquid formulations and the percent recovery of malic acid in nicotine malate liquid formulations.

Table 3

Analyte Measured	%Recovery
Nicotine (nicotine freebase liquid formulations)	80.2±1.3
Nicotine (nicotine benzoate liquid formulations)	90.4±3.4
Benzoic acid (nicotine benzoate liquid formulations)	91.8±3.5
Nicotine (nicotine malate liquid formulations)	92.1±4.9
malic acid (nicotine malate liquid formulations)	46.4±8.1

[00129] The percent recovery of malic acid was significantly lower than that of nicotine and benzoic acid, with a larger variability across sample replicates. Malic acid was reported to thermally decompose at 150°C, a temperature that is lower than common electronic cigarette operating temperature. The low recovery of malic acid found in the aerosol agrees with the thermal instability of malic acid. This leads to low effective nicotine to malic ratio in the aerosol compared to the ratio in the nicotine liquid formulation. Thus the protonation state of nicotine is also lower in the aerosol which will result in effectively less nicotine being present in the aerosol generated with a nicotine malate liquid formulation. Lower nicotine recovery in the case of freebase nicotine liquid formulation compared to the nicotine liquid formulations might result from the sample collection and assay procedure that small portion of gaseous nicotine escaped from the smoking system.

Volatile nicotine in aerosol

[00130] The amount of nicotine in the aerosol exiting the a low temperature vaporization device, i.e. an electronic cigarette, was examined by calculating percent nicotine captured in bubbler-1 compared to the total recovered nicotine. Benzoic acid is expected to reside in the particles (i.e. liquid droplets) in aerosol as it is non-volatile. Benzoic acid was thus used as a particle marker for nicotine since it is expected to protonate nicotine at 1:1 molar ratio, which will result in nicotine being present in the aerosol, in some embodiments in a non-gas phase of the aerosol. The amount of aerosolized nicotine was calculated by comparing the difference

between the amount of benzoic acid captured in bubbler-1 and the amount of benzoic acid in the nicotine liquid formulation.

[00131] A linear relationship was found between the amount of nicotine captured in bubbler-1 to the molar ratio of benzoic acid to nicotine in the nicotine liquid formulations (FIG. 9). At a 1:1 molar ratio of nicotine to benzoic acid, nicotine becomes fully protonated and the minimum amount of vapor collected in bubbler-1 was measured. Moreover, at a molar ratio of 1:1.5 of nicotine to benzoic acid, no further decrease in the amount of aerosolized nicotine was detected. It should also be noted that a higher percentage of freebase nicotine was collected by bubbler-1 indicating a higher concentration of gas phase nicotine was nicotine generated when using freebase nicotine in the nicotine liquid formulation.

[00132] Theoretically malic acid, which is diprotic, will protonate nicotine at a 0.5:1 molar ratio of malic acid to nicotine. However, malic acid is known to degrade at the operating temperature of the electronic cigarette resulting in a low transfer efficiency from the liquid formulation to the aerosol. Thus, given the low transfer efficiency of malic acid, the effective nicotine to malic ratio in the aerosol was 0.23 when generated using the nicotine liquid formulation comprising a molar ratio of 1:0.5 of nicotine to malic acid and 0.87 when generated using the nicotine liquid formulation comprising a molar ratio of 1:2 of nicotine to malic acid. As expected, the percent acid captured in bubbler-1 when using a nicotine liquid formulation comprising a 1:0.5 nicotine to malic acid molar ratio fell between the percent acid recovered when using nicotine liquid formulations comprising a nicotine to benzoic acid molar ratio of 1:0.4 and 1:0.7. The nicotine liquid formulation comprising a 1:2 molar ratio of nicotine to malic acid delivered an aerosol comprising a molar ratio of nicotine to malic acid of 1:0.87, thus containing excess malic acid than needed to fully protonate nicotine, leaving only 14.7% nicotine captured in bubbler-1 (FIG. 10).

[00133] Aerosolized nicotine that stays in particles is more likely to travel down to alveoli and get into the blood of a user. Gaseous nicotine has greater chance to deposit in upper respiratory tract and be absorbed at a different rate from deep lung gas exchange region. Thus, using nicotine liquid formulations with a molar ratio of 1:1 nicotine to benzoic acid or 1:2 nicotine to malic acid, about the same molar amount of aerosolized nicotine in the non-gas phase would be delivered to a user's lungs. This is in agreement with the $T_{\max}$ data described in Example 8.

Example 14: Acidic Functional Group Requirements Testing

[00134] The experimental system comprised a glass bubbler (bubbler-1), a Cambridge filter pad, and 2 glass bubblers (trap-1 and trap-2, connected in sequence) to trap any volatiles that pass through the filter pad. Low temperature electronic vaporization device, i.e. an electronic cigarette, was connected to the inlet of bubbler 1, and was activated by a smoking machine

connected to the outlet of trap 2 under designed puffing regime. The puffing regime comprised: Number of puffs per sample=30, puff size=60 cc, puff duration=4s. The trap solvent comprised 0.3% HCl in water. The nicotine liquid formulations tested were: freebase nicotine, nicotine benzoate at molar ratios of nicotine to acid of 1:0.4, 1:0.7, 1:1, and 1:1.5, and nicotine malate at molar ratios of nicotine to acid of 1:0.5 and 1:2. The formulations were generated using the procedures described in Example 1. In the experimental system gaseous (i.e. vapor) analytes were capture by the bubblers.

[00135] The procedure comprised:

- weighing the following parts prior to the start of puffing: the electronic cigarette filled with nicotine liquid formulation, the bubbler-1 filled with 35mL trap solvent, a clean filter pad and pad holder, the trap-1 filled with 20mL trap solvent, and trap-2 filled with 20mL trap solvent;
- connecting in the following sequence: the electronic cigarette, bubbler-1, the filter pad, trap-1, trap-2, and the smoking machine;
- smoking was conducted under the aforementioned puffing regime. A clean air puff of the same puff size and duration was done after each smoking puff;
- weighing all parts after the end of the puffing regime. The inlet tubing of bubbler-1 was assayed with 10mL of trap solvent in aliquots of 1mL. The total solvent amount in bubbler-1 after puffing was calculated with the correction of water loss from 60 puffs. The filter pad was cut in half and each half was extracted in 20mL trap solvent for 2 hours. The pad extract was filtered through 0.2 μ m Nylon syringe filter. The front half of the pad holder was assayed with 5mL trap solvent. The back half of the pad holder was assayed with 3mL trap solvent;
- analyzing solutions by UV-Vis spectroscopy. The absorbance at 259nm was used to calculate the nicotine concentration. The absorbance at 230nm was used to calculate the benzoic acid concentration. Malic acid was quantified using Malic acid UV test kit from NZYTech Inc.

Results and Discussions

[00136] The amount of nicotine in the aerosol exiting the a low temperature vaporization device, i.e. an electronic cigarette, was examined by calculating percent nicotine captured in bubbler-1 compared to the total recovered nicotine. Benzoic acid is expected to reside in the particles (i.e. liquid droplets) in aerosol as it is non-volatile. Benzoic acid was thus used as a particle marker for nicotine since it is expected to protonate nicotine at 1:1 molar ratio, which

will result in nicotine being present in the aerosol, in some embodiments in a non-gas phase of the aerosol. The amount of aerosolized nicotine was calculated by comparing the difference between the amount of benzoic acid captured in bubbler-1 and the amount of benzoic acid in the nicotine liquid formulation.

[00137] A linear relationship was found between the amount of nicotine captured in bubbler-1 to the molar ratio of benzoic acid to nicotine in the nicotine liquid formulations (FIG. 9). At a 1:1 molar ratio of nicotine to benzoic acid, nicotine becomes fully protonated and the minimum amount of vapor collected in bubbler-1 was measured. Moreover, at a molar ratio of 1:1.5 of nicotine to benzoic acid, no further decrease in the amount of aerosolized nicotine was detected. It should also be noted that a higher percentage of freebase nicotine was collected by bubbler-1 indicating a higher concentration of gas phase nicotine was nicotine generated when using freebase nicotine in the nicotine liquid formulation.

[00138] Benzoic acid and succinic acid have similar boiling points, 249°C for benzoic acid and 235°C for succinic acid, and both acids melt and evaporate without decomposition. Thus a nicotine liquid formulation generated using either acid should behave similarly and generate an aerosol with about the same molar amount of nicotine in aerosol. Thus, it is likely that the same total amount of acid will be collected when using either acid in the nicotine liquid formulation. Stated differently, it is likely that about the same percentage of succinic acid would be recovered when using a nicotine succinate liquid formulation in the electronic cigarette as compared to the percentage benzoic acid recovered when using a nicotine benzoate liquid formulation as described in Example 13. As such, the same percentage of nicotine will also likely be captured in bubbler-1 when using either succinic acid or benzoic acid in a nicotine liquid formulation.

[00139] Here different molar ratios of acidic functional groups to moles of nicotine were investigated. Since succinic acid is a diprotic acid, it was expected that a molar ratio of 1:0.25 of nicotine to succinic acid would result in the same amount of acid captured in bubbler-1 as captured using a 1:0.5 molar ratio of nicotine to benzoic acid. Further, it was expected that a molar ratio of 1:0.5 of nicotine to succinic acid would result in about the same amount of nicotine captured in bubbler-1 as captured using a 1:1 molar ratio of nicotine to benzoic acid. As was expected about the same percentage of acid was collected in bubbler-1 when using a molar ratio of 1:0.25 of nicotine to succinic acid in the nicotine liquid formulation as would be expected based on the amount of nicotine captured using a 1:0.4 and 1:0.7 nicotine to benzoic acid molar ratio nicotine liquid formulation (FIG. 11). Further, as was expected about the same percentage of acid was collected in bubbler-1 when using a molar ratio of 1:0.5 of nicotine to succinic acid in the nicotine liquid formulation compared to using a 1:1 molar ratio of nicotine to benzoic acid (FIG. 11).

[00140] Thus, since succinic acid is diprotic, one mole of succinic acid likely protonates two moles of nicotine thus stabilizing the two moles of nicotine in the aerosol. Stated differently, half the molar amount of succinic acid in a nicotine liquid formulation used in low temperature electronic vaporization device, i.e. an electronic cigarette, is needed to fully protonate nicotine and stabilize nicotine in the aerosol compared to using benzoic acid in a nicotine liquid formulation used in low temperature electronic vaporization device, i.e. an electronic cigarette. Moreover, it is plausible that succinic acid was ranked low in the satisfaction study described in Example 3 because excess succinic acid (1:2 molar ratio of nicotine to succinic acid) was included in the formulation and thus it is likely the excess succinic acid was delivered to the user thus resulting in an unfavorable experience for the user. For example, an unfavorable experience comprises a flavor, a nervous response, and/or an irritation of one or more of an oral cavity, an upper respiratory tract, and/or the lungs.

[00141] Further understanding may be gained through contemplation of the numbered embodiments below.

1. A method of delivering nicotine to a user comprising deploying low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine formulation comprising:
 - a. from about 0.5% (w/w) to about 20% (w/w) nicotine;
 - b. a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
 - c. a biologically acceptable liquid carrier,wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.
2. The method of embodiment 1, wherein a molar ratio of acidic functional groups to nicotine is from about 0.25:1 to about 4:1.
3. The method of any one of the embodiments 1-2, wherein the acid and nicotine form a nicotine salt.
4. The method of embodiment 1-7, wherein nicotine formulation comprises monoprotonated nicotine.
5. The method of any one of the embodiments 1-4, wherein the aerosol comprises monoprotonated nicotine.
6. The method of any one of the embodiments 1-5, wherein the aerosol is delivered to the user's lungs.
7. The method of embodiment 6, wherein the aerosol is delivered to alveoli in the user's lungs
8. The method of any one of the embodiments 1-10, wherein nicotine is stabilized in salt form in the aerosol.

9. The method of any one of the embodiments 1-10, wherein nicotine is carried in salt form in the aerosol.
10. The method of any one of the embodiments 1-9, wherein the acid comprises one carboxylic acid functional group.
11. The method of any one of the embodiments 1-9, wherein the acid comprises more than one carboxylic acid functional group.
12. The method of any one of the embodiments 1-9, wherein the acid is selected from the group consisting of: formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, citric acid, lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, phenylacetic acid, benzoic acid, pyruvic acid, levulinic acid, tartaric acid, lactic acid, malonic acid, succinic acid, fumaric acid, gluconic acid, saccharic acid, salicylic acid, sorbic acid, masonic acid, or malic acid.
13. The method of any one of the embodiments 1-9, wherein the acid comprises one or more of a carboxylic acid, a dicarboxylic acid, and a keto acid.
14. The method of any one of the embodiments 1-9, wherein the acid comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
15. The method of any one of the embodiments 1-9, wherein the acid comprises benzoic acid.
16. The method of any one of the embodiments 1-11, wherein the molar ratio of acid to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
17. The method of any one of the embodiments 1-11, wherein the molar ratio of acidic functional groups to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
18. The method of any one of the embodiments 1-11, wherein the molar ratio of acidic functional group hydrogens to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
19. The method of any one of the embodiments 1-11, wherein the molar ratio of acid to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1,

- about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
20. The method of any one of the embodiments 1-11, wherein the molar ratio of acidic functional groups to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
21. The method of any one of the embodiments 1-11, wherein the molar ratio of acidic functional groups hydrogens to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
22. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is about 0.5% (w/w), 1% (w/w), about 2% (w/w), about 3% (w/w), about 4% (w/w), about 5% (w/w), about 6% (w/w), about 7% (w/w), about 8% (w/w), about 9% (w/w), about 10% (w/w), about 11% (w/w), about 12% (w/w), about 13% (w/w), about 14% (w/w), about 15% (w/w), about 16% (w/w), about 17% (w/w), about 18% (w/w), about 19% (w/w), or about 20% (w/w).
23. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w), from about 0.5% (w/w) to about 18% (w/w), from about 0.5% (w/w) to about 15% (w/w), from about 0.5% (w/w) to about 12% (w/w), from about 0.5% (w/w) to about 10% (w/w), from about 0.5% (w/w) to about 8% (w/w), from about 0.5% (w/w) to about 7% (w/w), from about 0.5% (w/w) to about 6% (w/w), from about 0.5% (w/w) to about 5% (w/w), from about 0.5% (w/w) to about 4% (w/w), from about 0.5% (w/w) to about 3% (w/w), or from about 0.5% (w/w) to about 2% (w/w).
24. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 1% (w/w) to about 20% (w/w), from about 1% (w/w) to about 18% (w/w), from about 1% (w/w) to about 15% (w/w), from about 1% (w/w) to about 12% (w/w), from about 1% (w/w) to about 10% (w/w), from about 1% (w/w) to about 8% (w/w), from about 1% (w/w) to about 7% (w/w), from about 1% (w/w) to about 6% (w/w), from about 1% (w/w) to about 5% (w/w), from about 1% (w/w) to about 4% (w/w), from about 1% (w/w) to about 3% (w/w), or from about 1% (w/w) to about 2% (w/w).
25. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 2% (w/w) to about 20% (w/w), from about 2% (w/w) to about 18% (w/w), from

- about 2% (w/w) to about 15% (w/w), from about 2% (w/w) to about 12% (w/w), from about 2% (w/w) to about 10% (w/w), from about 2% (w/w) to about 8% (w/w), from about 2% (w/w) to about 7% (w/w), from about 2% (w/w) to about 6% (w/w), from about 2% (w/w) to about 5% (w/w), from about 2% (w/w) to about 4% (w/w), or from about 2% (w/w) to about 3% (w/w).
26. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 3% (w/w) to about 20% (w/w), from about 3% (w/w) to about 18% (w/w), from about 3% (w/w) to about 15% (w/w), from about 3% (w/w) to about 12% (w/w), from about 3% (w/w) to about 10% (w/w), from about 3% (w/w) to about 8% (w/w), from about 3% (w/w) to about 7% (w/w), from about 3% (w/w) to about 6% (w/w), from about 3% (w/w) to about 5% (w/w), or from about 3% (w/w) to about 4% (w/w).
27. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 4% (w/w) to about 20% (w/w), from about 4% (w/w) to about 18% (w/w), from about 4% (w/w) to about 15% (w/w), from about 4% (w/w) to about 12% (w/w), from about 4% (w/w) to about 10% (w/w), from about 4% (w/w) to about 8% (w/w), from about 4% (w/w) to about 7% (w/w), from about 4% (w/w) to about 6% (w/w), or from about 4% (w/w) to about 5% (w/w).
28. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 5% (w/w) to about 20% (w/w), from about 5% (w/w) to about 18% (w/w), from about 5% (w/w) to about 15% (w/w), from about 5% (w/w) to about 12% (w/w), from about 5% (w/w) to about 10% (w/w), from about 5% (w/w) to about 8% (w/w), from about 5% (w/w) to about 7% (w/w), or from about 5% (w/w) to about 6% (w/w).
29. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 6% (w/w) to about 20% (w/w), from about 6% (w/w) to about 18% (w/w), from about 6% (w/w) to about 15% (w/w), from about 6% (w/w) to about 12% (w/w), from about 6% (w/w) to about 10% (w/w), from about 6% (w/w) to about 8% (w/w), or from about 6% (w/w) to about 7% (w/w).
30. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is from about 2% (w/w) to about 6% (w/w).
31. The method of any one of the embodiments 1-[0054], wherein the nicotine concentration is about 5% (w/w).
32. The method of any one of the embodiments 1-[0072], wherein the molar concentration of nicotine in the aerosol is about the same as the molar concentration of the acid in the aerosol.
33. The method of any one of the embodiments 1-32, wherein the aerosol comprises about 50% of the nicotine in the formulation, about 60% of the nicotine in the formulation, about 70%

of the nicotine in the formulation, about 75% of the nicotine in the formulation, about 80% of the nicotine in the formulation, about 85% of the nicotine in the formulation, about 90% of the nicotine in the formulation, about 95% of the nicotine in the formulation, or about 99% of the nicotine in the formulation.

34. The method of any one of the embodiments 1-33, wherein the aerosol comprises condensate in particles sizes from about 0.1 microns to about 5 microns, from about 0.1 microns to about 4.5 microns, from about 0.1 microns to about 4 microns, from about 0.1 microns to about 3.5 microns, from about 0.1 microns to about 3 microns, from about 0.1 microns to about 2.5 microns, from about 0.1 microns to about 2 microns, from about 0.1 microns to about 1.5 microns, from about 0.1 microns to about 1 microns, from about 0.1 microns to about 0.9 microns, from about 0.1 microns to about 0.8 microns, from about 0.1 microns to about 0.7 microns, from about 0.1 microns to about 0.6 microns, from about 0.1 microns to about 0.5 microns, from about 0.1 microns to about 0.4 microns, from about 0.1 microns to about 0.3 microns, from about 0.1 microns to about 0.2 microns, or from about 0.3 to about 0.4 microns.
35. The method of embodiment 1-34, wherein the aerosol comprises condensate of nicotine salt.
36. The method of embodiment 1-34, wherein the aerosol comprises condensate comprising one or more of the carrier, nicotine salt, freebase nicotine, and free acid.
37. The method of embodiment 1-9, wherein the acid does not decompose at room temperature and does not decompose at the operating temperature of the electronic cigarette.
38. The method of any one of the embodiments 1-37, wherein an operating temperature is from 150 °C to 250 °C.
39. The method of any one of the embodiments 1-37, wherein an operating temperature is from 180 °C to 220 °C.
40. The method of any one of the embodiments 1-37, wherein an operating temperature is about 200 °C.
41. The method of any one of embodiments 1-40, wherein the acid is stable at and below operating temperature or about 200 °C.
42. The method of any one of embodiments 1-40, wherein the acid does not decompose at and below operating temperature or about 200 °C.
43. The method of any one of embodiments 1-40, wherein the acid does not oxidize at and below operating temperature or about 200 °C.
44. The method of any one of embodiments 1-43, wherein the formulation is non-toxic to a user of the electronic cigarette.
45. The method of any one of the embodiments 1-44, wherein the formulation is non-corrosive

to the electronic cigarette.

46. The method of any one of the embodiments 1-45, wherein the formulation comprises a flavorant.
47. The method of any one of the embodiments 1-46, wherein inhaling the aerosol over a period of five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 1 min to about 8 min.
48. The method of embodiment 47, wherein the nicotine plasma Tmax is from about 1 min to about 7 min, from about 1 min to about 6 min, from about 1 min to about 5 min, from about 1 min to about 4 min, from about 1 min to about 3 min, from about 1 min to about 2 min, from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, about 2 min, or about 1 min.
49. The method of any one of the embodiments 1-46, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 2 min to about 8 min.
50. The method of embodiment 49, wherein the nicotine plasma Tmax is from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, or about 2 min.

51. The method of any one of the embodiments 1-46, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 min to about 8 min.
52. The method of embodiment 51, wherein the nicotine plasma Tmax is from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 8 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, or about 3 min.
53. The method of any one of the embodiments 1-46, wherein the Tmax is less than about 8 min.
54. The method of any one of the embodiments 47-53, wherein the Tmax is determined based on at least three independent data sets.
55. The method of embodiment 47-53, wherein the Tmax is a range of at least three independent data sets.
56. The method of embodiment 47-53, wherein the Tmax is an average $\pm$ a standard deviation of at least three independent data sets.
57. The method of any one of the embodiments 1-56, wherein the liquid carrier comprises glycerol, propylene glycol, trimethylene glycol, water, ethanol or a combination thereof.
58. The method of any one of the embodiments 1-56, wherein the liquid carrier comprises propylene glycol and vegetable glycerin.
59. The method of any one of the embodiments 1-56, wherein the liquid carrier comprises 20% to 50% of propylene glycol and 80% to 50% of vegetable glycerin.
60. The method of any one of the embodiments 1-56, wherein the liquid carrier comprises 30% propylene glycol and 70% vegetable glycerin.
61. The method of any one of embodiments 1-17, wherein the formulation further comprises one or more additional acids.
62. The method of embodiment 21, wherein the one or more additional acids comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
63. The method of embodiment 21, wherein the one or more additional acids comprises benzoic acid.
64. The method of any one of the embodiments 21-63, wherein the one or more additional acids

forms one or more additional nicotine salts.

65. A method of delivering nicotine to a user comprising deploying low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine formulation comprising:

- a. from about 0.5% (w/w) to about 20% (w/w) nicotine;
- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

66. A method of delivering nicotine to a user comprising deploying low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine formulation comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

67. A method of delivering nicotine to a user comprising deploying low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine formulation comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 1:1 to about 2:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

68. A method of delivering nicotine to a user comprising deploying low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine formulation

comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. a molar ratio of benzoic acid to nicotine of about 1:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

69. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette,, the formulation comprising:

- a. from about 0.5% (w/w) to about 20% (w/w) nicotine;
- b. a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

70. The formulation of embodiment 69, wherein a molar ratio of acidic functional groups to nicotine is from about 1:1 to about 4:1.

71. The formulation of any one of the embodiments 69-70, wherein the acid and nicotine form a nicotine salt.

72. The formulation of embodiment 69-71, comprising monoprotonated nicotine.

73. The formulation of any one of the embodiments 69-72, wherein the aerosol comprises monoprotonated nicotine.

74. The formulation of any one of the embodiments 69-73, wherein the aerosol is delivered to the user's lungs.

75. The formulation of embodiment 74, wherein the aerosol is delivered to alveoli in the user's lungs

76. The formulation of any one of the embodiments 69-75, wherein nicotine is stabilized in salt form in the aerosol.

77. The formulation of any one of the embodiments 69-75, wherein nicotine is carried in salt form in the aerosol.

78. The formulation of any one of the embodiments 69-77, wherein the acid comprises one carboxylic acid functional group.

79. The formulation of any one of the embodiments 69-77, wherein the acid comprises more than one carboxylic acid functional group.

80. The formulation of any one of the embodiments 69-77, wherein the acid is selected from the group consisting of: formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, citric acid, lauric acid, myristic acid, palmitic acid,

stearic acid, oleic acid, linoleic acid, linolenic acid, phenylacetic acid, benzoic acid, pyruvic acid, levulinic acid, tartaric acid, lactic acid, malonic acid, succinic acid, fumaric acid, gluconic acid, saccharic acid, salicylic acid, sorbic acid, maseonic acid, or malic acid.

81. The formulation of any one of the embodiments 69-77, wherein the acid comprises one or more of a carboxylic acid, a dicarboxylic acid, and a keto acid.
82. The formulation of any one of the embodiments 69-77, wherein the acid comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
83. The formulation of any one of the embodiments 69-77, wherein the acid comprises nicotine benzoate.
84. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acid to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
85. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acidic functional groups to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
86. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acidic functional group hydrogens to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
87. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acid to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
88. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acidic functional groups to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.

89. The formulation of any one of the embodiments 69-83, wherein the molar ratio of acidic functional group hydrogens to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
90. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w), from about 0.5% (w/w) to about 18% (w/w), from about 0.5% (w/w) to about 15% (w/w), from about 0.5% (w/w) to about 12% (w/w), from about 0.5% (w/w) to about 10% (w/w), from about 0.5% (w/w) to about 8% (w/w), from about 0.5% (w/w) to about 7% (w/w), from about 0.5% (w/w) to about 6% (w/w), from about 0.5% (w/w) to about 5% (w/w), from about 0.5% (w/w) to about 4% (w/w), from about 0.5% (w/w) to about 3% (w/w), or from about 0.5% (w/w) to about 2% (w/w).
91. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is about 0.5% (w/w), about 1% (w/w), about 2% (w/w), about 3% (w/w), about 4% (w/w), about 5% (w/w), about 6% (w/w), about 7% (w/w), about 8% (w/w), about 9% (w/w), about 10% (w/w), about 11% (w/w), about 12% (w/w), about 13% (w/w), about 14% (w/w), about 15% (w/w), about 16% (w/w), about 17% (w/w), about 18% (w/w), about 19% (w/w), or about 20% (w/w).
92. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 1% (w/w) to about 20% (w/w), from about 1% (w/w) to about 18% (w/w), from about 1% (w/w) to about 15% (w/w), from about 1% (w/w) to about 12% (w/w), from about 1% (w/w) to about 10% (w/w), from about 1% (w/w) to about 8% (w/w), from about 1% (w/w) to about 7% (w/w), from about 1% (w/w) to about 6% (w/w), from about 1% (w/w) to about 5% (w/w), from about 1% (w/w) to about 4% (w/w), from about 1% (w/w) to about 3% (w/w), or from about 1% (w/w) to about 2% (w/w).
93. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 2% (w/w) to about 20% (w/w), from about 2% (w/w) to about 18% (w/w), from about 2% (w/w) to about 15% (w/w), from about 2% (w/w) to about 12% (w/w), from about 2% (w/w) to about 10% (w/w), from about 2% (w/w) to about 8% (w/w), from about 2% (w/w) to about 7% (w/w), from about 2% (w/w) to about 6% (w/w), from about 2% (w/w) to about 5% (w/w), from about 2% (w/w) to about 4% (w/w), or from about 2% (w/w) to about 3% (w/w).
94. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 3% (w/w) to about 20% (w/w), from about 3% (w/w) to about 18% (w/w), from about 3% (w/w) to about 15% (w/w), from about 3% (w/w) to about 12% (w/w), from about

- 3% (w/w) to about 10% (w/w), from about 3% (w/w) to about 8% (w/w), from about 3% (w/w) to about 7% (w/w), from about 3% (w/w) to about 6% (w/w), from about 3% (w/w) to about 5% (w/w), or from about 3% (w/w) to about 4% (w/w).
95. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 4% (w/w) to about 20% (w/w), from about 4% (w/w) to about 18% (w/w), from about 4% (w/w) to about 15% (w/w), from about 4% (w/w) to about 12% (w/w), from about 4% (w/w) to about 10% (w/w), from about 4% (w/w) to about 8% (w/w), from about 4% (w/w) to about 7% (w/w), from about 4% (w/w) to about 6% (w/w), or from about 4% (w/w) to about 5% (w/w).
96. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 5% (w/w) to about 20% (w/w), from about 5% (w/w) to about 18% (w/w), from about 5% (w/w) to about 15% (w/w), from about 5% (w/w) to about 12% (w/w), from about 5% (w/w) to about 10% (w/w), from about 5% (w/w) to about 8% (w/w), from about 5% (w/w) to about 7% (w/w), or from about 5% (w/w) to about 6% (w/w).
97. The formulation of any one of the embodiments 69-87, wherein the nicotine concentration is from about 6% (w/w) to about 20% (w/w), from about 6% (w/w) to about 18% (w/w), from about 6% (w/w) to about 15% (w/w), from about 6% (w/w) to about 12% (w/w), from about 6% (w/w) to about 10% (w/w), from about 6% (w/w) to about 8% (w/w), or from about 6% (w/w) to about 7% (w/w).
98. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is from about 2% (w/w) to about 6% (w/w).
99. The formulation of any one of the embodiments 69-89, wherein the nicotine concentration is about 5% (w/w).
100. The formulation of any one of the embodiments 69-99, wherein the molar concentration of nicotine in the aerosol is about the same as the molar concentration of the acid in the aerosol.
101. The formulation of any one of the embodiments 69-100, wherein the aerosol comprises about 50% of the nicotine in the formulation, about 60% of the nicotine in the formulation, about 70% of the nicotine in the formulation, about 75% of the nicotine in the formulation, about 80% of the nicotine in the formulation, about 85% of the nicotine in the formulation, about 90% of the nicotine in the formulation, about 95% of the nicotine in the formulation, or about 99% of the nicotine in the formulation.
102. The formulation of any one of the embodiments 69-101, wherein the aerosol comprises condensate in particles sizes from about 0.1 microns to about 5 microns, from about 0.1 microns to about 4.5 microns, from about 0.1 microns to about 4 microns, from about 0.1

microns to about 3.5 microns, from about 0.1 microns to about 3 microns, from about 0.1 microns to about 2.5 microns, from about 0.1 microns to about 2 microns, from about 0.1 microns to about 1.5 microns, from about 0.1 microns to about 1 microns, from about 0.1 microns to about 0.9 microns, from about 0.1 microns to about 0.8 microns, from about 0.1 microns to about 0.7 microns, from about 0.1 microns to about 0.6 microns, from about 0.1 microns to about 0.5 microns, from about 0.1 microns to about 0.4 microns, from about 0.1 microns to about 0.3 microns, from about 0.1 microns to about 0.2 microns, or from about 0.3 to about 0.4 microns.

103. The formulation of embodiment 69-102, wherein the aerosol comprises condensate of nicotine salt.
104. The formulation of embodiment 69-102, wherein the aerosol comprises condensate comprising one or more of the carrier, nicotine salt, freebase nicotine, and free acid.
105. The formulation of embodiment 69-104, wherein the acid does not decompose at room temperature and does not decompose at the operating temperature of the electronic cigarette.
106. The formulation of any one of the embodiments 69-105, wherein an operating temperature of the electronic cigarette is from 150 °C to 250 °C.
107. The formulation of any one of the embodiments 69-105, wherein an operating temperature of the electronic cigarette is from 180 °C to 220 °C.
108. The formulation of any one of the embodiments 69-105, wherein an operating temperature of the electronic cigarette is about 200 °C.
109. The formulation of any one of embodiments 69-108, wherein the acid is stable at and below operating temperature of the electronic cigarette or about 200 °C.
110. The formulation of any one of embodiments 69-108, wherein the acid does not decompose at and below operating temperature of the electronic cigarette or about 200 °C.
111. The formulation of any one of embodiments 69-108, wherein the acid does not oxidize at and below operating temperature of the electronic cigarette or about 200 °C.
112. The formulation of any one of embodiments 69-108, wherein the formulation is non-toxic to a user of the electronic cigarette.
113. The formulation of any one of the embodiments 69-112, wherein the formulation is non-corrosive to the electronic cigarette.
114. The formulation of any one of the embodiments 69-113, wherein the formulation comprises a flavorant.
115. The formulation of any one of the embodiments 69-114, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 1 min to about 8 min.

116. The formulation of embodiment 115, wherein the nicotine plasma Tmax is from about 1 min to about 7 min, from about 1 min to about 6 min, from about 1 min to about 5 min, from about 1 min to about 4 min, from about 1 min to about 3 min, from about 1 min to about 2 min, from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, about 2 min, or about 1 min.
117. The formulation of any one of the embodiments 69-114, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 2 min to about 8 min.
118. The formulation of embodiment 117, wherein the nicotine plasma Tmax is from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, or about 2 min.
119. The formulation of any one of the embodiments 69-114, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 min to about 8 min.
120. The formulation of embodiment 119, wherein the nicotine plasma Tmax is from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 8 min, from about 4 min to

- about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, or about 3 min.
121. The formulation of any one of the embodiments 69-114, wherein the Tmax is less than about 8 min.
122. The formulation of any one of the embodiments 115-121, wherein the Tmax is determined based on at least three independent data sets.
123. The formulation of embodiment 115-121, wherein the Tmax is a range of at least three independent data sets.
124. The formulation of embodiment 115-121, wherein the Tmax is an average $\pm$ a standard deviation of at least three independent data sets.
125. The formulation of any one of the embodiments 69-124, wherein the liquid carrier comprises glycerol, propylene glycol, trimethylene glycol, water, ethanol or a combination thereof.
126. The formulation of any one of the embodiments 69-124, wherein the liquid carrier comprises propylene glycol and vegetable glycerin.
127. The formulation of any one of the embodiments 69-124, wherein the liquid carrier comprises 20% to 50% of propylene glycol and 80% to 50% of vegetable glycerin.
128. The formulation of any one of the embodiments 69-124, wherein the liquid carrier comprises 30% propylene glycol and 70% vegetable glycerin.
129. The formulation of any one of embodiments 69-128, further comprising one or more additional acids.
130. The formulation of any one of embodiment 129, wherein the one or more additional acids comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
131. The formulation of embodiment 129, wherein the one or more additional acids comprises benzoic acid.
132. The formulation of any one of the embodiments 129-131, wherein the one or more additional acids forms one or more additional nicotine salts.
133. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, the formulation comprising:
- a. from about 0.5% (w/w) to about 20% (w/w) nicotine;

- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
 - c. a biologically acceptable liquid carrier,
- wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.
134. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette,, the formulation comprising:
- a. from about 2% (w/w) to about 6% (w/w) nicotine;
 - b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
 - c. a biologically acceptable liquid carrier,
- wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.
135. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette,, the formulation comprising:
- a. from about 2% (w/w) to about 6% (w/w) nicotine;
 - b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 1:1 to about 2:1; and
 - c. a biologically acceptable liquid carrier,
- wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.
136. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette,, the formulation comprising:
- a. from about 2% (w/w) to about 6% (w/w) nicotine;
 - b. a molar ratio of benzoic acid to nicotine of about 1:1; and
 - c. a biologically acceptable liquid carrier,
- wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.
137. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a fluid compartment configured to be in fluid

communication with a heating element, the fluid compartment comprising a nicotine formulation comprising:

- a. from about 0.5% (w/w) to about 20% (w/w) nicotine;
- b. a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of nicotine in the formulation.

138. The cartridge of embodiment 137, wherein a molar ratio of acidic functional groups to nicotine is from about 1:1 to about 4:1.
139. The cartridge of any one of the embodiments 137-138, wherein the acid and nicotine form a nicotine salt.
140. The cartridge of embodiment 137-139, wherein nicotine formulation comprises monoprotonated nicotine.
141. The cartridge of any one of the embodiments 137-140, wherein the aerosol comprises monoprotonated nicotine.
142. The cartridge of any one of the embodiments 137-141, wherein the aerosol is delivered to the user's lungs.
143. The cartridge of embodiment 142, wherein the aerosol is delivered to alveoli in the user's lungs.
144. The cartridge of any one of the embodiments 137-143, wherein nicotine is stabilized in salt form in the aerosol.
145. The cartridge of any one of the embodiments 137-143, wherein nicotine is carried in salt form in the aerosol.
146. The cartridge of any one of the embodiments 137-145, wherein the acid comprises one carboxylic acid functional group.
147. The cartridge of any one of the embodiments 137-145, wherein the acid comprises more than one carboxylic acid functional group.
148. The cartridge of any one of the embodiments 137-145, wherein the acid is selected from the group consisting of: formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, citric acid, lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, phenylacetic acid, benzoic acid, pyruvic acid, levulinic acid, tartaric acid, lactic acid, malonic acid, succinic acid, fumaric acid, gluconic acid, saccharic acid, salicylic acid, sorbic acid, masonic acid, or malic acid.
149. The cartridge of any one of the embodiments 137-145, wherein the acid comprises one or more of a carboxylic acid, a dicarboxylic acid, and a keto acid.

150. The cartridge of any one of the embodiments 137-145, wherein the acid comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
151. The cartridge of any one of the embodiments 137-145, wherein the acid comprises benzoic acid.
152. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acid to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
153. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acidic functional groups to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
154. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acidic functional group hydrogens to nicotine in the formulation is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
155. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acid to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
156. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acidic functional groups to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.
157. The cartridge any one of the embodiments 137-151, wherein the molar ratio of acidic functional group hydrogens to nicotine in the aerosol is about 0.25:1, about 0.3:1, about 0.4:1, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1, about 1:1, about 1.2:1, about 1.4:1, about 1.6:1, about 1.8:1, about 2:1, about 2.2:1, about 2.4:1, about 2.6:1, about 2.8:1, about 3:1, about 3.2:1, about 3.4:1, about 3.6:1, about 3.8:1, or about 4:1.

158. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is about 0.5% (w/w), about 1% (w/w), about 2% (w/w), about 3% (w/w), about 4% (w/w), about 5% (w/w), about 6% (w/w), about 7% (w/w), about 8% (w/w), about 9% (w/w), about 10% (w/w), about 11% (w/w), about 12% (w/w), about 13% (w/w), about 14% (w/w), about 15% (w/w), about 16% (w/w), about 17% (w/w), about 18% (w/w), about 19% (w/w), or about 20% (w/w).
159. The cartridge of any one of the embodiments 137-157, wherein the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w), from about 0.5% (w/w) to about 18% (w/w), from about 0.5% (w/w) to about 15% (w/w), from about 0.5% (w/w) to about 12% (w/w), from about 0.5% (w/w) to about 10% (w/w), from about 0.5% (w/w) to about 8% (w/w), from about 0.5% (w/w) to about 7% (w/w), from about 0.5% (w/w) to about 6% (w/w), from about 0.5% (w/w) to about 5% (w/w), from about 0.5% (w/w) to about 4% (w/w), from about 0.5% (w/w) to about 3% (w/w), or from about 0.5% (w/w) to about 2% (w/w).
160. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 1% (w/w) to about 20% (w/w), from about 1% (w/w) to about 18% (w/w), from about 1% (w/w) to about 15% (w/w), from about 1% (w/w) to about 12% (w/w), from about 1% (w/w) to about 10% (w/w), from about 1% (w/w) to about 8% (w/w), from about 1% (w/w) to about 7% (w/w), from about 1% (w/w) to about 6% (w/w), from about 1% (w/w) to about 5% (w/w), from about 1% (w/w) to about 4% (w/w), from about 1% (w/w) to about 3% (w/w), or from about 1% (w/w) to about 2% (w/w).
161. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 2% (w/w) to about 20% (w/w), from about 2% (w/w) to about 18% (w/w), from about 2% (w/w) to about 15% (w/w), from about 2% (w/w) to about 12% (w/w), from about 2% (w/w) to about 10% (w/w), from about 2% (w/w) to about 8% (w/w), from about 2% (w/w) to about 7% (w/w), from about 2% (w/w) to about 6% (w/w), from about 2% (w/w) to about 5% (w/w), from about 2% (w/w) to about 4% (w/w), or from about 2% (w/w) to about 3% (w/w).
162. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 3% (w/w) to about 20% (w/w), from about 3% (w/w) to about 18% (w/w), from about 3% (w/w) to about 15% (w/w), from about 3% (w/w) to about 12% (w/w), from about 3% (w/w) to about 10% (w/w), from about 3% (w/w) to about 8% (w/w), from about 3% (w/w) to about 7% (w/w), from about 3% (w/w) to about 6% (w/w), from about 3% (w/w) to about 5% (w/w), or from about 3% (w/w) to about 4% (w/w).
163. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration

- is from about 4% (w/w) to about 20% (w/w), from about 4% (w/w) to about 18% (w/w), from about 4% (w/w) to about 15% (w/w), from about 4% (w/w) to about 12% (w/w), from about 4% (w/w) to about 10% (w/w), from about 4% (w/w) to about 8% (w/w), from about 4% (w/w) to about 7% (w/w), from about 4% (w/w) to about 6% (w/w), or from about 4% (w/w) to about 5% (w/w).
164. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 5% (w/w) to about 20% (w/w), from about 5% (w/w) to about 18% (w/w), from about 5% (w/w) to about 15% (w/w), from about 5% (w/w) to about 12% (w/w), from about 5% (w/w) to about 10% (w/w), from about 5% (w/w) to about 8% (w/w), from about 5% (w/w) to about 7% (w/w), or from about 5% (w/w) to about 6% (w/w).
165. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 6% (w/w) to about 20% (w/w), from about 6% (w/w) to about 18% (w/w), from about 6% (w/w) to about 15% (w/w), from about 6% (w/w) to about 12% (w/w), from about 6% (w/w) to about 10% (w/w), from about 6% (w/w) to about 8% (w/w), or from about 6% (w/w) to about 7% (w/w).
166. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is from about 2% (w/w) to about 6% (w/w).
167. The cartridge any one of the embodiments 137-157, wherein the nicotine concentration is about 5% (w/w).
168. The cartridge any one of the embodiments 137-167, wherein the molar concentration of nicotine in the aerosol is about the same as the molar concentration of the acid in the aerosol.
169. The cartridge of any one of the embodiments 137-168, wherein the aerosol comprises about 50% of the nicotine in the formulation, about 60% of the nicotine in the formulation, about 70% of the nicotine in the formulation, about 75% of the nicotine in the formulation, about 80% of the nicotine in the formulation, about 85% of the nicotine in the formulation, about 90% of the nicotine in the formulation, about 95% of the nicotine in the formulation, or about 99% of the nicotine in the formulation.
170. The cartridge of any one of the embodiments 137-169, wherein the aerosol comprises condensate in particles sizes from about 0.1 microns to about 5 microns, from about 0.1 microns to about 4.5 microns, from about 0.1 microns to about 4 microns, from about 0.1 microns to about 3.5 microns, from about 0.1 microns to about 3 microns, from about 0.1 microns to about 2.5 microns, from about 0.1 microns to about 2 microns, from about 0.1 microns to about 1.5 microns, from about 0.1 microns to about 1 microns, from about 0.1 microns to about 0.9 microns, from about 0.1 microns to about 0.8 microns, from about 0.1 microns to about 0.7 microns, from about 0.1 microns to about 0.6 microns, from about 0.1

microns to about 0.5 microns, from about 0.1 microns to about 0.4 microns, from about 0.1 microns to about 0.3 microns, from about 0.1 microns to about 0.2 microns, or from about 0.3 to about 0.4 microns.

171. The cartridge of embodiment 137-170, wherein the aerosol comprises condensate of nicotine salt.
172. The cartridge of embodiment 137-170, wherein the aerosol comprises condensate comprising one or more of the carrier, nicotine salt, freebase nicotine, and free acid.
173. The cartridge of embodiment 137-172, wherein the acid does not decompose at room temperature and does not decompose at the operating temperature of the electronic cigarette.
174. The cartridge of any one of the embodiments 137-173, wherein an operating temperature is from 150 °C to 250 °C.
175. The cartridge of any one of the embodiments 137-173, wherein an operating temperature is from 180 °C to 220 °C.
176. The cartridge any one of the embodiments 137-173, wherein an operating temperature is about 200 °C.
177. The cartridge of any one of embodiments 137-176, wherein the acid is stable at and below operating temperature or about 200 °C.
178. The cartridge of any one of embodiments 137-176, wherein the acid does not decompose at and below operating temperature or about 200 °C.
179. The cartridge of any one of embodiments 137-176, wherein the acid does not oxidize at and below operating temperature or about 200 °C.
180. The cartridge of any one of embodiments 137-179, wherein the formulation is non-toxic to a user of the electronic cigarette.
181. The cartridge of any one of the embodiments 137-180, wherein the formulation is non-corrosive to the electronic cigarette.
182. The cartridge of any one of the embodiments 137-181, wherein the formulation comprises a flavorant.
183. The cartridge of any one of the embodiments 137-182, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 1 min to about 8 min.
184. The cartridge of embodiment 183, wherein the nicotine plasma Tmax is from about 1 min to about 7 min, from about 1 min to about 6 min, from about 1 min to about 5 min, from about 1 min to about 4 min, from about 1 min to about 3 min, from about 1 min to about 2 min, from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about

- 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, about 2 min, or about 1 min.
185. The cartridge of any one of the embodiments 137-182, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 2 min to about 8 min.
186. The cartridge of embodiment 185, wherein the nicotine plasma Tmax is from about 2 min to about 8 min, from about 2 min to about 7 min, from about 2 min to about 6 min, from about 2 min to about 5 min, from about 2 min to about 4 min, from about 2 min to about 3 min, from about 3 min to about 8 min, from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, less than about 3 min, less than about 2 min, less than about 1 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, about 3 min, or about 2 min.
187. The cartridge of any one of the embodiments 137-182, wherein inhaling the aerosol over a period of about five minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 min to about 8 min.
188. The cartridge of embodiment 187, wherein the nicotine plasma Tmax is from about 3 min to about 7 min, from about 3 min to about 6 min, from about 3 min to about 5 min, from about 3 min to about 4 min, from about 4 min to about 8 min, from about 4 min to about 7 min, from about 4 min to about 6 min, from about 4 min to about 5 min, from about 5 min to about 8 min, from about 5 min to about 7 min, from about 5 min to about 6 min, from about 6 min to about 8 min, from about 6 min to about 7 min, from about 7 min to about 8 min, less than about 8 min, less than about 7 min, less than about 6 min, less than about 5 min, less than about 4 min, about 8 min, about 7 min, about 6 min, about 5 min, about 4 min, or

about 3 min.

189. The cartridge of any one of the embodiments 137-182, wherein the Tmax is less than about 8 min.
190. The cartridge of any one of the embodiments 183-189, wherein the Tmax is determined based on at least three independent data sets.
191. The cartridge of embodiment 183-189, wherein the Tmax is a range of at least three independent data sets.
192. The cartridge of embodiment 183-189, wherein the Tmax is an average $\pm$ a standard deviation of at least three independent data sets.
193. The cartridge of any one of the embodiments 137-192, wherein the liquid carrier comprises glycerol, propylene glycol, trimethylene glycol, water, ethanol or a combination thereof.
194. The cartridge of any one of the embodiments 137-192, wherein the liquid carrier comprises propylene glycol and vegetable glycerin.
195. The cartridge of any one of the embodiments 137-192, wherein the liquid carrier comprises 20% to 50% of propylene glycol and 80% to 50% of vegetable glycerin.
196. The cartridge of any one of the embodiments 137-192, wherein the liquid carrier comprises 30% propylene glycol and 70% vegetable glycerin.
197. The cartridge of any one of embodiments 137-196, wherein the formulation further comprises one or more additional acids.
198. The cartridge of embodiment 197, wherein the one or more additional acids comprises one or more of benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
199. The cartridge of embodiment 197, wherein the one or more additional acids comprises nicotine benzoic acid.
200. The cartridge of any one of the embodiments 197-199, wherein the one or more additional acids forms one or more additional nicotine salts.
201. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a fluid compartment configured to be in fluid communication with a heating element, the fluid compartment comprising a nicotine formulation comprising:
 - a. from about 0.5% (w/w) to about 20% (w/w) nicotine;
 - b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1;

and

- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

202. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a fluid compartment configured to be in fluid communication with a heating element, the fluid compartment comprising a nicotine formulation comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 0.25:1 to about 4:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

203. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a fluid compartment configured to be in fluid communication with a heating element, the fluid compartment comprising a nicotine formulation comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. an acid selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid, wherein the a molar ratio of acid to nicotine from about 1:1 to about 2:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at least a portion of the nicotine in the formulation.

204. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a fluid compartment configured to be in fluid communication with a heating element, the fluid compartment comprising a nicotine formulation comprising:

- a. from about 2% (w/w) to about 6% (w/w) nicotine;
- b. a molar ratio of benzoic acid to nicotine of about 1:1; and
- c. a biologically acceptable liquid carrier,

wherein operation of the electronic cigarette generates an inhalable aerosol comprising at

least a portion of the nicotine in the formulation.

[00142] Although preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein can be employed in practicing the invention. It is intended that the following embodiments define the scope of the invention and that methods and structures within the scope of these embodiments and their equivalents be covered thereby.

WHAT IS CLAIMED IS:

What is claimed is:

1. A method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises said nicotine, an acid, and a biologically acceptable liquid carrier, wherein using the electronic cigarette comprises:
 - providing an amount of said nicotine liquid formulation to said heater;
 - said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
2. The method of any one of the claims 1, wherein said amount comprises about 4 μ L of said nicotine liquid formulation.
3. The method of any one of the claims 1, wherein said amount comprises about 4.5 mg of said nicotine liquid formulation.
4. The method of any one of the claims 1-3, wherein a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w).
5. The method of any one of the claims 1-4, wherein a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1.
6. The method of any one of the claims 1-5, wherein said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1.
7. The method of any one of the claims claim 1-6, wherein said acid and said nicotine form a nicotine salt.
8. The method of any one of the claims 7, wherein said nicotine is stabilized in said nicotine salt in said inhalable aerosol.
9. The method of claim 7, wherein said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt.
10. The method of any one of claims 1-9, wherein one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user.
11. The method of any one of the claims 1-10, wherein said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid.
12. The method of any one of the claims 1-10, wherein said acid is selected from the group

consisting of: benzoic acid, pyruvic acid, and salicylic acid.

13. The method of any one of the claims 1-10, wherein said acid is benzoic acid.
14. The method of any one of the claims 1-13, wherein said concentration is from about 2% (w/w) to about 6% (w/w).
15. The method of any one of the claims 1-13, wherein said concentration is about 5% (w/w).
16. The method of any one of the claims 1-15, wherein said biologically acceptable liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin.
17. The method of any one of the claims 1-15, wherein said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin.
18. The method of any one of the claims 1-17, wherein said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C.
19. The method of any one of the claims 1-17, wherein said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C.
20. The method of any one of the claims 1-17, wherein said heater heats said amount of said nicotine liquid formulation to about 200 °C.
21. The method of any one of claims 1-20, wherein said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
22. The method of claim 21 wherein said additional acid forms an additional nicotine salt.
23. The method of any one of the claims 1-22, wherein at least about 60% to about 90% of said acid in said amount is in said aerosol.
24. The method of any one of the claims 1-22, wherein at least about 70% to about 90% of said acid in said amount is in said aerosol.
25. The method of any one of the claims 1-22, wherein at least about 80% to about 90% of said acid in said amount is in said aerosol.
26. The method of any one of the claims 1-22, wherein more than about 90% of said acid in said amount is in said aerosol.
27. A method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises:
 - a. said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w);
 - b. an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and

- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater;
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

28. A method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises:

- a. nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to a heater;
- the heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

29. A method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises:

- a. nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to a heater;
- the heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

30. A method of generating an inhalable aerosol comprising nicotine for delivery to a user comprising using low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a nicotine liquid formulation and a heater, wherein the nicotine liquid formulation comprises:
- a. nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
 - b. benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and
 - c. a biologically acceptable liquid carrier;
- wherein using the electronic cigarette comprises:
- providing an amount of said nicotine liquid formulation to a heater;
 - the heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said benzoic acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
31. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising said nicotine, an acid, and a biologically acceptable liquid carrier, wherein using said electronic cigarette comprises:
- providing an amount of said nicotine liquid formulation to said heater;
 - said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
32. The cartridge of any one of the claims 31, wherein said amount comprises about 4 μ L of said nicotine liquid formulation.
33. The cartridge of any one of the claims 31, wherein said amount comprises about 4.5 mg of said nicotine liquid formulation.
34. The cartridge of any one of the claims 31-33, wherein a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w).
35. The cartridge of any one of the claims 31-34, wherein a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1.
36. The cartridge of any one of the claims 31-35, wherein said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1.

37. The cartridge of any one of the claims claim 31-36, wherein said acid and said nicotine form a nicotine salt.
38. The cartridge of any one of the claims 37, wherein said nicotine is stabilized in said nicotine salt in said inhalable aerosol.
39. The cartridge of claim 37, wherein said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt.
40. The cartridge of any one of claims 31-39, wherein one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user.
41. The cartridge of any one of the claims 31-40, wherein said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid.
42. The cartridge of any one of the claims 31-40, wherein said acid is selected from the group consisting of: benzoic acid, pyruvic acid, and salicylic acid.
43. The cartridge of any one of the claims 31-40, wherein said acid is benzoic acid.
44. The cartridge of any one of the claims 31-43, wherein said concentration is from about 2% (w/w) to about 6% (w/w).
45. The cartridge of any one of the claims 31-43, wherein said concentration is about 5% (w/w).
46. The cartridge of any one of the claims 31-45, wherein said biologically acceptable liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin.
47. The cartridge of any one of the claims 31-45, wherein said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin.
48. The cartridge of any one of the claims 31-47, wherein said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C.
49. The cartridge of any one of the claims 31-47, wherein said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C.
50. The cartridge of any one of the claims 31-47, wherein said heater heats said amount of said nicotine liquid formulation to about 200 °C.
51. The cartridge of any one of claims 31-50, wherein said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
52. The cartridge of claim 21 wherein said additional acid forms an additional nicotine salt.
53. The cartridge of any one of the claims 31-52, wherein at least about 60% to about 90% of said acid in said amount is in said aerosol.
54. The cartridge of any one of the claims 31-52, wherein at least about 70% to about 90% of

said acid in said amount is in said aerosol.

55. The cartridge of any one of the claims 31-52, wherein at least about 80% to about 90% of said acid in said amount is in said aerosol.
56. The cartridge of any one of the claims 31-52, wherein more than about 90% of said acid in said amount is in said aerosol.
57. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising:
- said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w);
 - an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and
 - a biologically acceptable liquid carrier;
- wherein using said electronic cigarette comprises:
- providing an amount of said nicotine liquid formulation to said heater;
 - said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
58. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising:
- said nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
 - an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
 - a biologically acceptable liquid carrier;
- wherein using said electronic cigarette comprises:
- providing an amount of said nicotine liquid formulation to said heater;
 - said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
59. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid

communication with a heating element, said fluid compartment comprising a nicotine formulation comprising:

- a. said nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
- c. a biologically acceptable liquid carrier;

wherein using said electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater;
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

60. A cartridge for use with low temperature electronic vaporization device, i.e. an electronic cigarette,, said cartridge comprising a fluid compartment configured to be in fluid communication with a heating element, said fluid compartment comprising a nicotine formulation comprising:

- a. said nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and
- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to a heater;
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said benzoic acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

61. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising nicotine, an acid, and a biologically acceptable liquid carrier, wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater;
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

62. The formulation of any one of the claims 61, wherein said amount comprises about 4 μ L of

said nicotine liquid formulation.

63. The formulation of any one of the claims 61, wherein said amount comprises about 4.5 mg of said nicotine liquid formulation.
64. The formulation of any one of the claims 61-63, wherein a concentration of said nicotine is from about 0.5% (w/w) to about 20% (w/w).
65. The formulation of any one of the claims 61-64, wherein a molar ratio of said acid to said nicotine is from about 0.25:1 to about 4:1.
66. The formulation of any one of the claims 61-65, wherein said acid comprises one or more acidic functional groups, and wherein a molar ratio of said acidic functional groups to said nicotine is from about 0.25:1 to about 4:1.
67. The formulation of any one of the claims claim 61-66, wherein said acid and said nicotine form a nicotine salt.
68. The formulation of any one of the claims 67, wherein said nicotine is stabilized in said nicotine salt in said inhalable aerosol.
69. The formulation of claim 67, wherein said inhalable aerosol comprises one or more of said nicotine, said acid, said carrier, and said nicotine salt.
70. The formulation of any one of claims 61-69, wherein one or more particles of said inhalable aerosol are sized for delivery to alveoli in a lung of said user.
71. The formulation of any one of the claims 61-70, wherein said acid is selected from the group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, succinic acid, and citric acid.
72. The formulation of any one of the claims 61-70, wherein said acid is selected from the group consisting of: benzoic acid, pyruvic acid, and salicylic acid.
73. The formulation of any one of the claims 61-70, wherein said acid is benzoic acid.
74. The formulation of any one of the claims 61-73, wherein said concentration is from about 2% (w/w) to about 6% (w/w).
75. The formulation of any one of the claims 61-73, wherein said concentration is about 5% (w/w).
76. The formulation of any one of the claims 61-75, wherein said biologically acceptable liquid carrier comprises from about 20% to about 50% of propylene glycol and from about 80% to about 50% of vegetable glycerin.
77. The formulation of any one of the claims 61-75, wherein said biologically acceptable liquid carrier comprises about 30% propylene glycol and about 70% vegetable glycerin.
78. The formulation of any one of the claims 61-77, wherein said heater heats said amount of said nicotine liquid formulation from about 150 °C to about 250 °C.

79. The formulation of any one of the claims 61-77, wherein said heater heats said amount of said nicotine liquid formulation from about 180 °C to about 220 °C.
80. The formulation of any one of the claims 61-77, wherein said heater heats said amount of said nicotine liquid formulation to about 200 °C.
81. The formulation of any one of claims 61-80, wherein said nicotine liquid formulation further comprises an additional acid selected from said group consisting of: benzoic acid, pyruvic acid, salicylic acid, levulinic acid, malic acid, succinic acid, and citric acid.
82. The formulation of claim 81 wherein said additional acid forms an additional nicotine salt.
83. The formulation of any one of the claims 61-82, wherein at least about 60% to about 90% of said acid in said amount is in said aerosol.
84. The formulation of any one of the claims 61-82, wherein at least about 70% to about 90% of said acid in said amount is in said aerosol.
85. The formulation of any one of the claims 61-82, wherein at least about 80% to about 90% of said acid in said amount is in said aerosol.
86. The formulation of any one of the claims 61-82, wherein more than about 90% of said acid in said amount is in said aerosol.
87. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising:
- said nicotine at a concentration from about 0.5% (w/w) to about 20% (w/w);
 - an acid at a molar ratio of said acid to said nicotine from about 0.25:1 to about 4:1; and
 - a biologically acceptable liquid carrier;
- wherein using the electronic cigarette comprises:
- providing an amount of said nicotine liquid formulation to said heater; and
 - said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.
88. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising:
- nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
 - an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
 - a biologically acceptable liquid carrier;
- wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater; and
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 50% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

89. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising:

- a. nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. an acid at a molar ratio of said acid to said nicotine from about 1:1 to about 4:1; and
- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater; and
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

90. A formulation for use in low temperature electronic vaporization device, i.e. an electronic cigarette, comprising a heater, the formulation comprising:

- a. nicotine at a concentration from about 2% (w/w) to about 6% (w/w);
- b. benzoic acid at a molar ratio of said benzoic acid to said nicotine of about 1:1; and
- c. a biologically acceptable liquid carrier;

wherein using the electronic cigarette comprises:

- providing an amount of said nicotine liquid formulation to said heater; and
- said heater forming an aerosol by heating said amount of said nicotine liquid formulation, wherein at least about 90% of said acid in said amount is in said aerosol, and wherein at least about 90% of said nicotine in said amount is in said aerosol.

FIG. 1

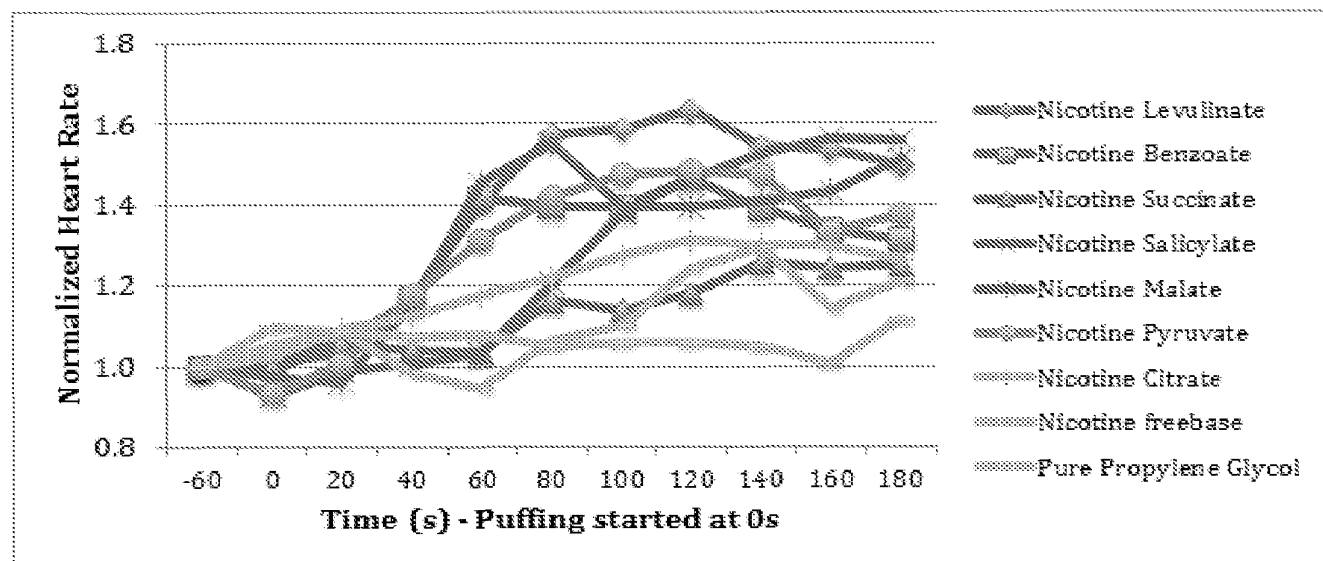


FIG. 2

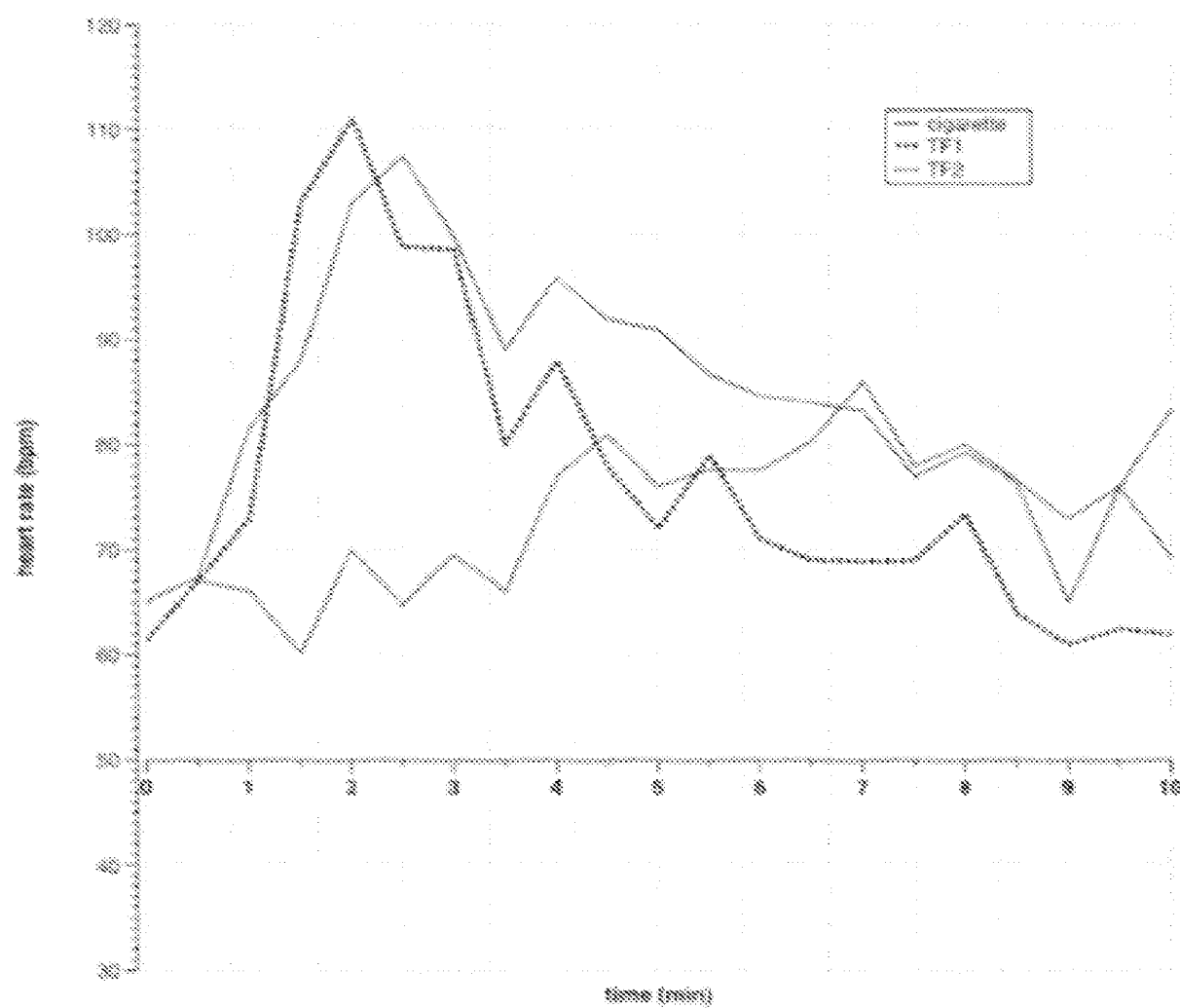


FIG. 3

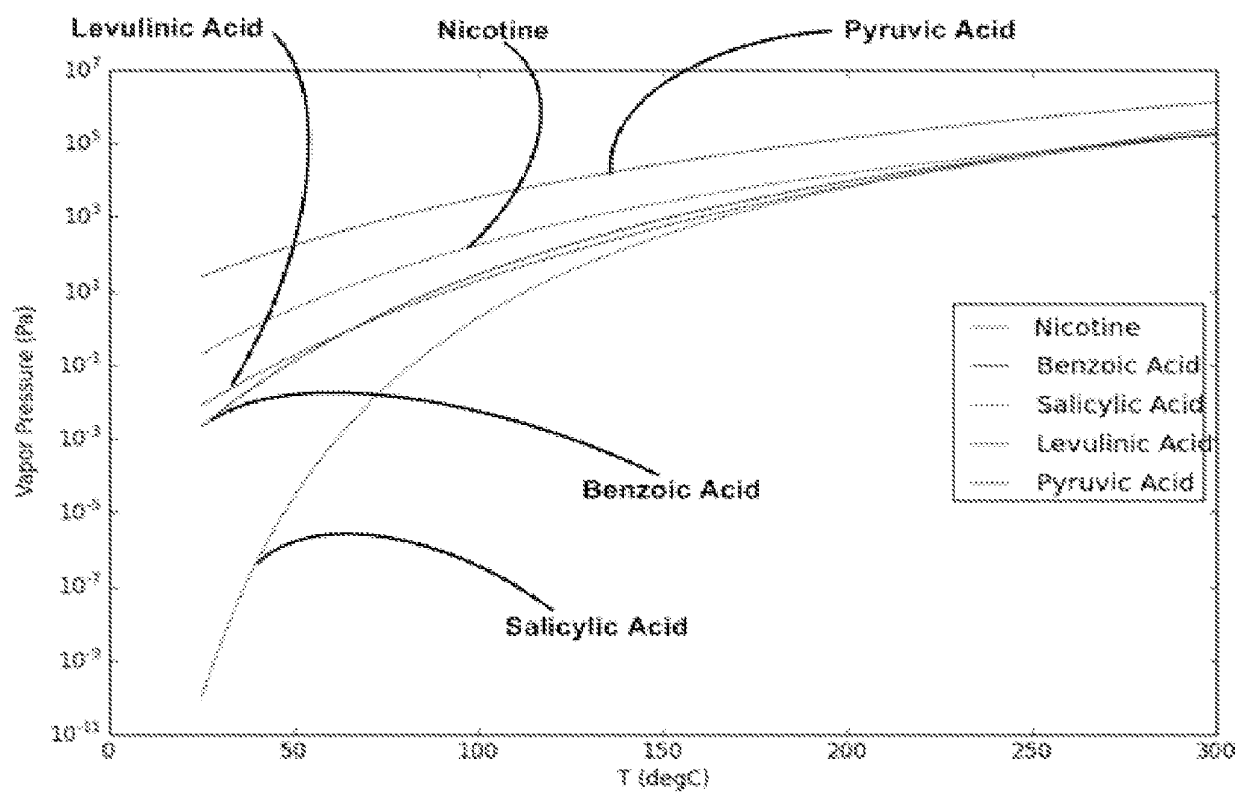
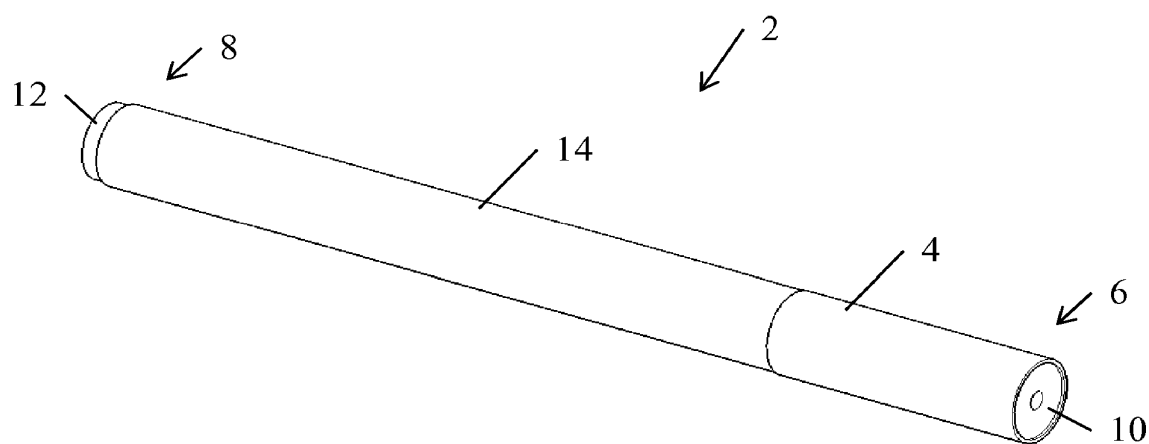


FIG. 4



4/7

FIG. 5

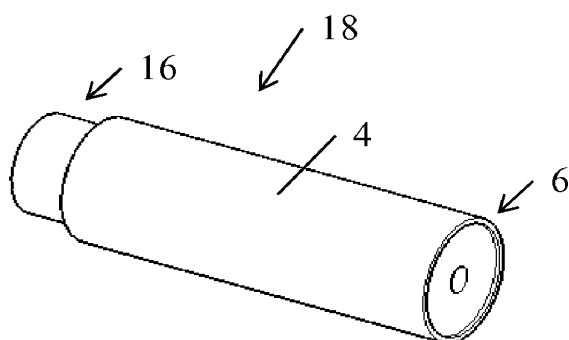


FIG. 6

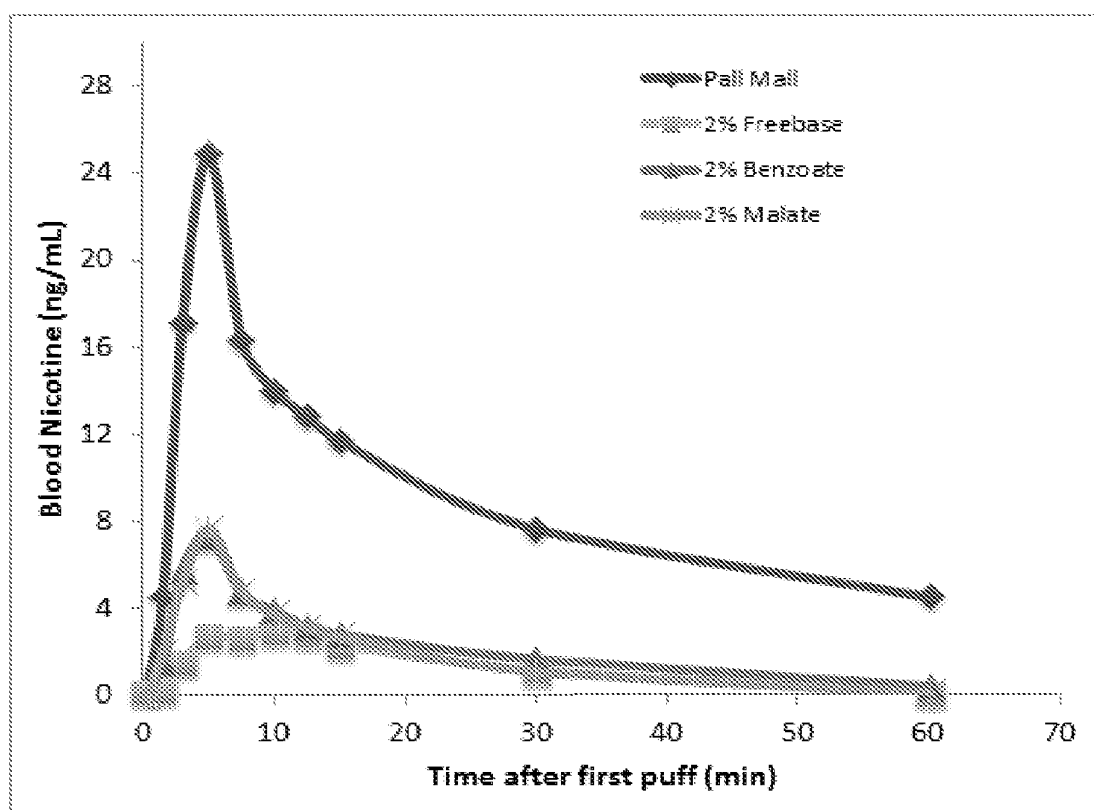


FIG. 7

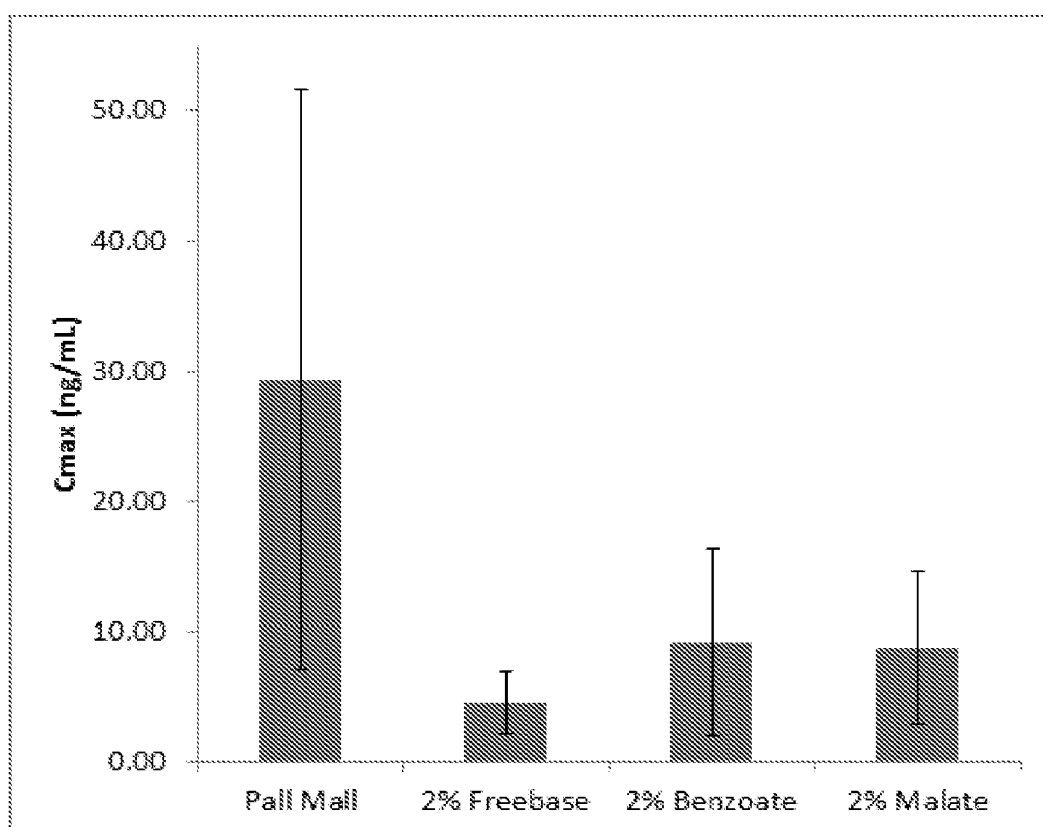


FIG. 8

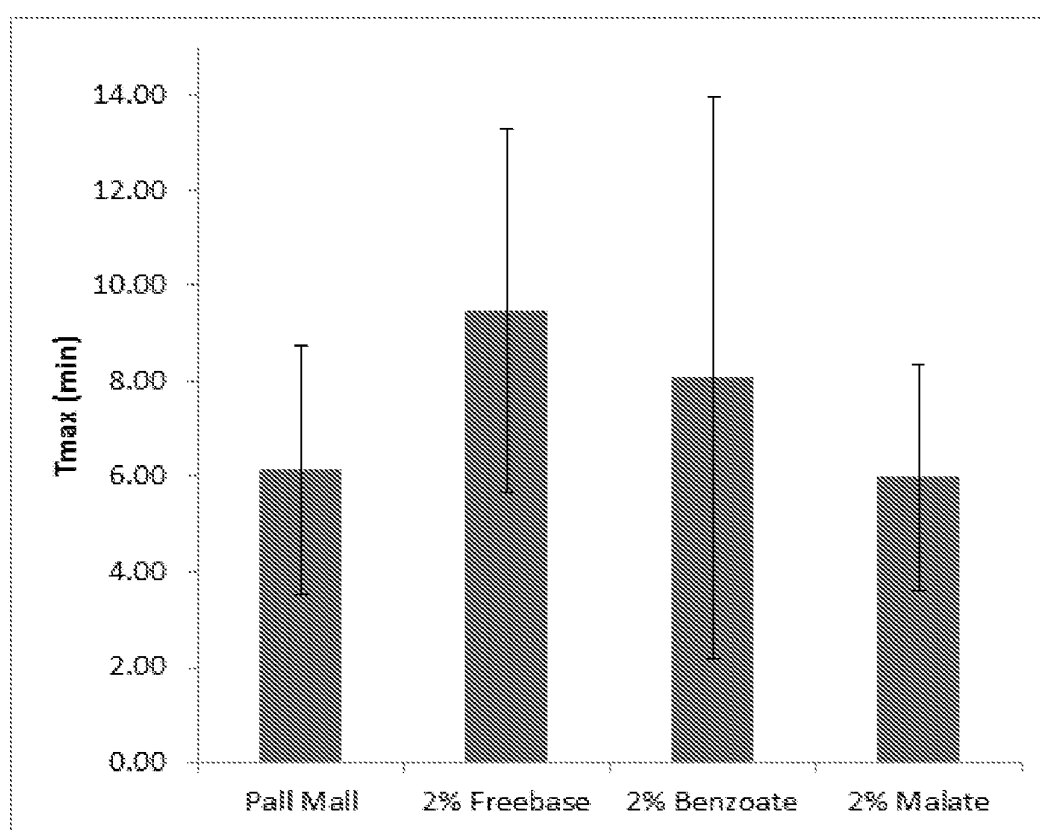


FIG. 9

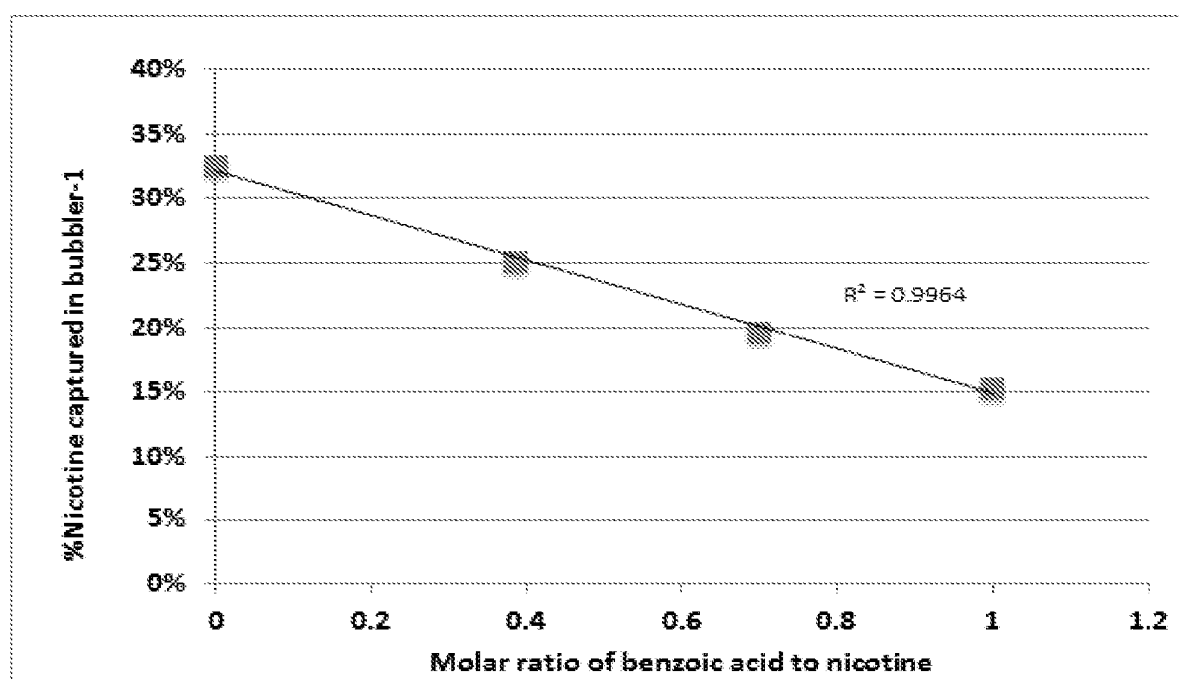


FIG. 10

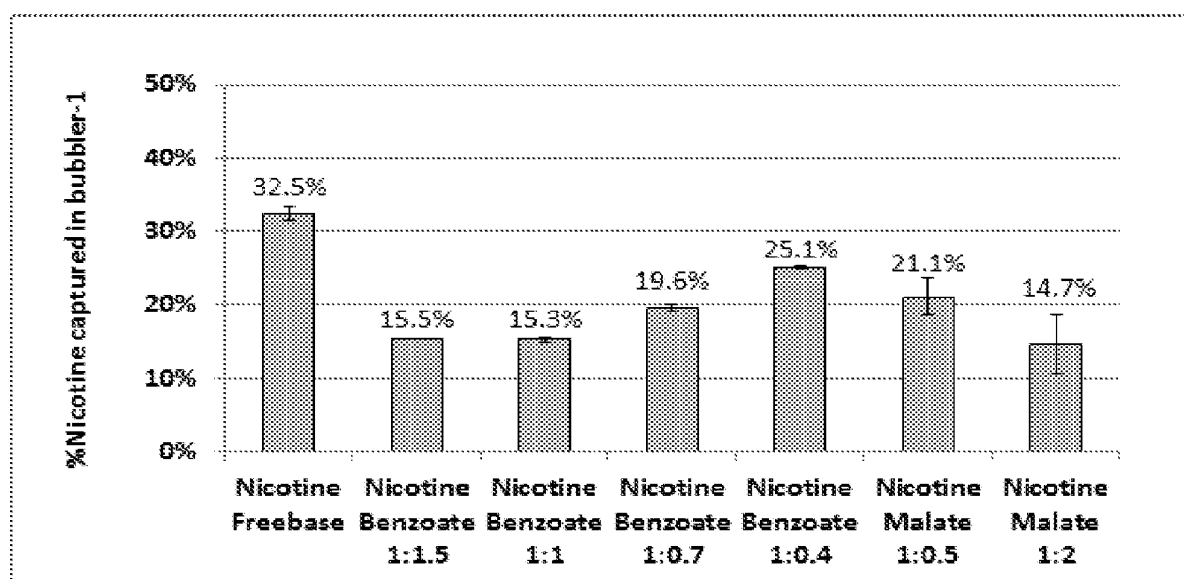
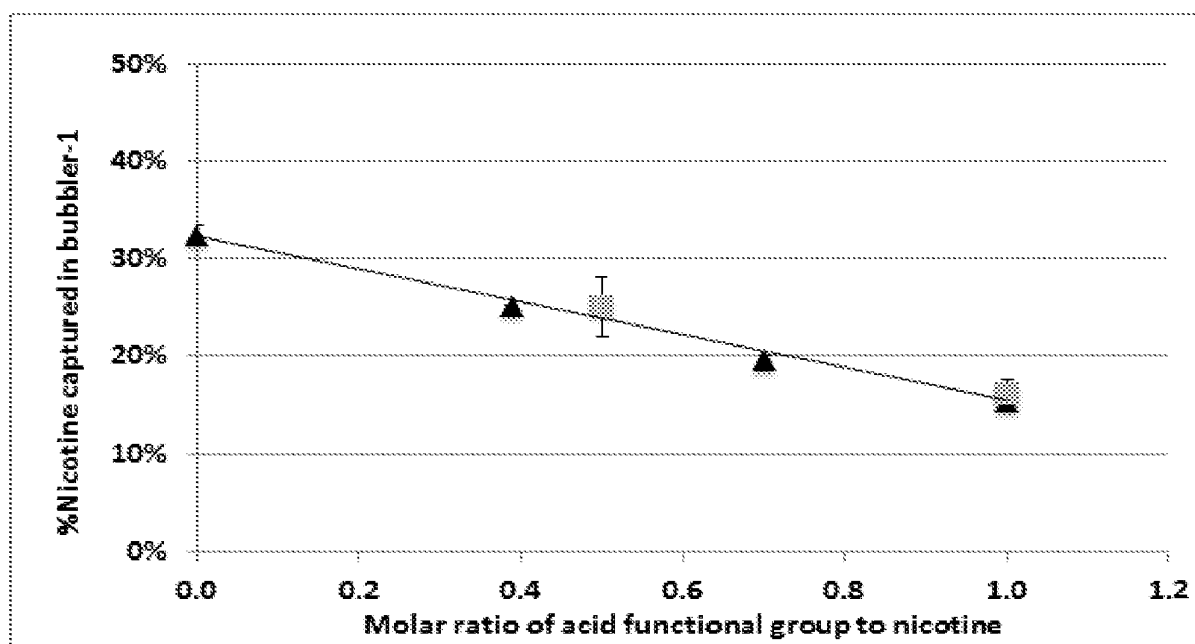


FIG. 11



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/064690

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A24F 1/10 (2014.01)

CPC - A24F 1/10 (2014.11)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A24F 1/10; A61K 31/465; A61P 25/34 (2014.01)

CPC - A24F 1/10; A61K 9/006, 31/465 (2014.11) (keyword delimited)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 128/202.21; 131/273, 330; 514/343 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Orbit, Google Patents, Google

Search terms used: nicotine, acid, heat, cigarette

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0236562 A1 (HEARN et al) 23 September 2010 (23.09.2010) entire document	1-4, 27-34, 57-64, 87-90
A	WO 03/055486 A1 (PHARMACIA AB) 10 July 2003 (10.07.2003) entire document	1-4, 27-34, 57-64, 87-90

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30 December 2014

Date of mailing of the international search report

18 FEB 2015

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-3201

Authorized officer:

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/064690

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 5-26, 35-56, 65-86
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (July 2009)



(51) International Patent Classification:
A24F 47/00 (2006.01)

(21) International Application Number:
PCT/EP2014/079496

(22) International Filing Date:
31 December 2014 (31.12.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
14150025.6 2 January 2014 (02.01.2014) EP

(71) Applicant: PHILIP MORRIS PRODUCTS S.A.
[CH/CH]; Quai Jeanrenaud 3, CH-2000 Neuchâtel (CH).

(72) Inventors: BUEHLER, Frederic Ulysse; Rue de l'Evoile
36, CH-2000 Neuchâtel (CH). EMMETT, Robert; Rue
des Poudrières 97, CH-2000 Neuchâtel (CH).

(74) Agent: MILLBURN, Julie; Reddie & Grose LLP, 16
Theobalds Road, London Greater London WC1X 8PL
(GB).

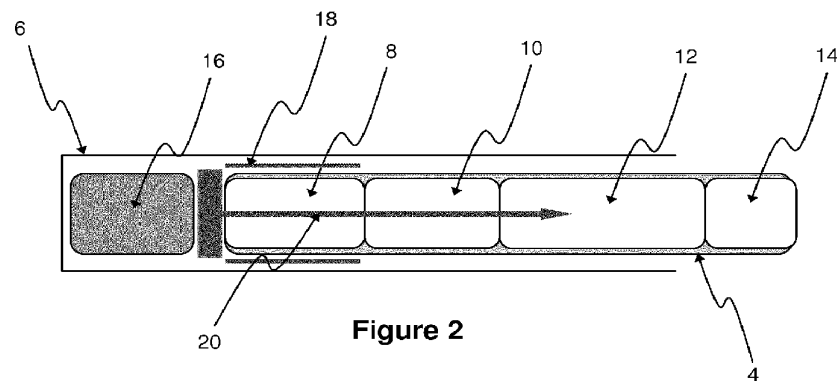
(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,
SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ,
TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU,
TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: AEROSOL-GENERATING SYSTEM COMPRISING A CYLINDRICAL POLYMERIC CAPSULE



(57) Abstract: An aerosol-generating system comprises: a nicotine source (8); a volatile delivery enhancing compound source (10), wherein the volatile delivery enhancing compound comprises an acid; and a heating means (18) for heating one or both of the nicotine source (8) and the volatile delivery enhancing compound source (10). One or both of the nicotine source (8) and the volatile delivery enhancing compound source (10) is encapsulated in a cylindrical polymeric capsule (2). The cylindrical polymeric capsule comprises a thermally conductive material.

AEROSOL-GENERATING SYSTEM COMPRISING A CYLINDRICAL POLYMERIC CAPSULE

The present invention relates to an aerosol-generating system comprising a nicotine source and a volatile delivery enhancing compound source. In particular, the present invention relates to an aerosol-generating system comprising a nicotine source and a volatile delivery enhancing compound source for generating an aerosol comprising nicotine salt particles.

Devices for delivering nicotine to a user comprising a nicotine source and a volatile delivery enhancing compound source are known. For example, WO 2008/121610 A1 discloses devices in which nicotine and a volatile delivery enhancing compound are reacted with one another in the gas phase to form an aerosol of nicotine salt particles that is inhaled by the user.

Exemplary Device 2 disclosed in WO 2008/121610 A1 comprises a delivery enhancing compound source 30 and a nicotine source 40 having frangible barrier end caps 35 and 45 heat sealed on the ends. As shown in Fig. 4 of WO 2008/121610 A1, the delivery enhancing compound source 30 and the nicotine source 40 are inserted into a first housing 50 through opposed open ends thereof. The first housing 50, containing the delivery enhancing compound source 30 and the nicotine source 40, is then inserted into a second housing 100. WO 2008/121610 A1 discloses that the first and second housings 50, 100 and the delivery enhancing compound source 30 and the nicotine source 40 are generally extruded plastic tubing. WO 2008/121610 A1 does not provide any information concerning the composition of the frangible barrier end caps 35 and 45.

Nicotine sources and volatile delivery enhancing compound sources for use in aerosol-generating systems of the type disclosed in WO 2008/121610 A1 will have a tendency to lose nicotine and volatile delivery enhancing compound, respectively, when stored for any length of time.

It would be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 in which the retention of one or both of the nicotine and the volatile delivery enhancing compound during storage is improved. In particular, it would be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 in which sufficient nicotine and volatile delivery enhancing compound is retained during storage to generate a desired aerosol of nicotine salt particles for delivery to a user upon use of the aerosol-generating system.

It would also be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 in which one or both of the nicotine and the volatile delivery enhancing compound are retained during storage without degradation by oxidation, hydrolysis or other unwanted reactions, which may alter the properties of the reactants.

It would further be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 in which one or both of the nicotine and the volatile delivery enhancing compound is released only upon use of the aerosol-generating system.

WO 2008/121610 A1 does not address how to optimize the ratio of nicotine and volatile delivery enhancing compound in the gas phase to minimize the amount of unreacted nicotine vapour and delivery enhancing compound vapour delivered to a user.

For example, where the vapour pressure of the volatile delivery enhancing compound is different from the vapour pressure of nicotine, this can lead to a difference in the vapour concentration of the two reactants. A difference in the vapour concentration of the volatile delivery enhancing compound and nicotine can lead to the delivery of unreacted delivery enhancing compound vapour to a user.

It is desirable to produce a maximum quantity of nicotine salt particles for delivery to a user using a minimum quantity of reactants. Consequently, it would be desirable to provide an aerosol-generating system of the type disclosed in WO 2008/121610 A1 that further improves the formation of an aerosol of nicotine salt particles for delivery to a user. It is especially desirable to increase the proportion of the gas phase volatile delivery enhancing compound that is reacted with the gas phase nicotine.

According to the invention there is provided an aerosol-generating system comprising: a nicotine source; a volatile delivery enhancing compound source, wherein the volatile delivery enhancing compound comprises an acid; and a heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source, wherein one or both of the nicotine source and the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material.

According to the invention there is also provided an aerosol-generating system comprising: an aerosol-generating article comprising a nicotine source and a volatile delivery enhancing compound source, wherein the volatile delivery enhancing compound comprises an acid, wherein one or both of the nicotine source and the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material; and an aerosol-generating device configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article, wherein the aerosol-generating device comprises heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source.

According to the invention there is further provided use of a cylindrical polymeric capsule comprising a thermally conductive material in an aerosol-generating system for generating a nicotine-containing aerosol comprising a heating means.

As used herein, by "encapsulated" it is meant that the cylindrical polymeric capsule forms a barrier or shell around the nicotine source or the volatile delivery enhancing compound source.

As used herein, the terms "cylinder" and "cylindrical" refer to a substantially right circular cylinder with a pair of opposed substantially planar end faces.

As used herein, the term “aerosol-generating device” refers to a device that interacts with an aerosol-generating article to generate an aerosol that is directly inhalable into a user’s lungs through the user’s mouth.

As used herein, the term “aerosol-generating article” refers to an article comprising an aerosol-forming substrate capable of releasing volatile compounds, which can form an aerosol. In particular, the term “aerosol-generating article” refers to an article comprising a nicotine source and a delivery enhancing compound source capable of releasing nicotine and a delivery enhancing compound that can react with one another in the gas phase to form an aerosol.

Aerosol-generating systems according to the invention comprise a proximal end through which, in use, an aerosol exits the aerosol-generating system for delivery to a user. The proximal end may also be referred to as the mouth end. In use, a user draws on the proximal end of the aerosol-generating article in order to inhale an aerosol generated by the aerosol-generating system. The aerosol-generating system comprises a distal end opposed to the proximal end.

As used herein, the term “longitudinal” is used to describe the direction between the proximal end and the opposed distal end of aerosol-generating systems and components of aerosol-generating systems according to the invention and the term “transverse” is used to describe the direction perpendicular to the longitudinal direction.

As used herein, by “length” is meant the maximum longitudinal dimension between the distal end and the proximal end of components, or portions of components, of aerosol-generating systems according to the invention.

As used herein, by “diameter” is meant the maximum transverse dimension of components, or portions of components, of aerosol-generating systems according to the invention.

As used herein, the terms “upstream” and “downstream” are used to describe the relative positions of components, or portions of components, of aerosol-generating systems according to the invention with respect to the direction of airflow through the aerosol-generating system when a user draws on the proximal end of the aerosol-generating system.

When a user draws on the proximal end of the aerosol-generating system, air is drawn into the aerosol-generating system, passes downstream through the aerosol-generating system and exits the aerosol-generating system at the proximal end.

The proximal end of aerosol-generating systems according to the invention may also be referred to as the downstream end and components, or portions of components, of aerosol-generating systems according to the invention may be described as being upstream or downstream of one another based on their positions relative to the airflow through the aerosol-generating system towards the proximal end.

One or both of the nicotine source and the volatile delivery enhancing compound source may be encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material.

5 In certain preferred embodiments, the nicotine source and the volatile delivery enhancing compound source are both encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material. In such embodiments, the nicotine source is encapsulated in a first cylindrical polymeric capsule and the volatile delivery enhancing compound source is encapsulated in a second cylindrical polymeric capsule.

10 Encapsulating one or both of the nicotine source and the volatile delivery enhancing compound source in a cylindrical polymeric capsule advantageously substantially reduces or prevents reaction of the nicotine and the volatile delivery enhancing compound with one another prior to use of the aerosol-generating system.

15 Where the nicotine source is encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule substantially reduces or prevents evaporation and loss of nicotine from the nicotine source prior to use of the aerosol-generating system. This advantageously improves retention of the nicotine during storage of aerosol-generating systems according to the invention.

20 The cylindrical polymeric capsule also isolates the nicotine source from exposure to external atmospheric effects and so substantially reduces or prevents reaction of the nicotine with atmospheric oxygen and water prior to use of the aerosol-generating system. This advantageously improves the stability of the nicotine during storage of aerosol-generating systems according to the invention.

25 Preferably, the cylindrical polymeric capsule forms a barrier or shell around the nicotine source that prevents contact of the nicotine with the atmosphere. In certain embodiments, the cylindrical polymeric capsule may form a barrier or shell around the nicotine source that prevents contact of the nicotine with the atmosphere and reduces or prevents exposure of the nicotine to light.

30 Preferably, the cylindrical polymeric capsule forms a barrier or shell around the nicotine source that provides an environment for the nicotine such that the nicotine remains stable upon storage at ambient temperature for a period of at least two months, more preferably for a period of at least four months.

35 Where the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule substantially reduces or prevents evaporation and loss of volatile delivery enhancing compound from the volatile delivery enhancing compound source prior to use of the aerosol-generating system. This advantageously improves retention of the volatile delivery enhancing compound during storage of aerosol-generating systems according to the invention.

The cylindrical polymeric capsule also isolates the volatile delivery enhancing compound source from exposure to external atmospheric effects and so substantially reduces or prevents reaction of the volatile delivery enhancing compound with atmospheric oxygen and water prior to use of the aerosol-generating system. This advantageously improves the stability of the volatile delivery enhancing compound during storage of aerosol-generating systems according to the invention.

Preferably, the cylindrical polymeric capsule forms a barrier or shell around the volatile delivery enhancing compound source that prevents contact of the volatile delivery enhancing compound with the atmosphere. In certain embodiments, the cylindrical polymeric capsule may form a barrier or shell around the volatile delivery enhancing compound source that prevents contact of the volatile delivery enhancing compound with the atmosphere and reduces or prevents exposure of the volatile delivery enhancing compound to light.

Preferably, the cylindrical polymeric capsule forms a barrier or shell around the volatile delivery enhancing compound source that provides an environment for the volatile delivery enhancing compound such that the volatile delivery enhancing compound remains stable upon storage at ambient temperature for a period of at least two months, more preferably for a period of at least four months.

Where the nicotine source is encapsulated in a cylindrical polymeric capsule, the nicotine can be released from the nicotine source when desired by piercing or otherwise opening the cylindrical polymeric capsule in which the nicotine source is encapsulated. Alternatively or in addition, where the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule, the volatile delivery enhancing compound can be released from the volatile delivery enhancing compound source when desired by piercing or otherwise opening the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated. This allows reaction between the nicotine and the volatile delivery enhancing compound in the gas phase to form an aerosol for inhalation by the user.

The cylindrical polymeric capsule may be a two-part capsule.

The cylindrical polymeric capsule may comprise a cylindrical body portion and a removable lid portion. In such embodiments, the cylindrical body portion comprises a first substantially planar end face of the cylindrical polymeric capsule and the removable lid portion comprises an opposed second substantially planar end face of the cylindrical polymeric capsule.

The cylindrical polymeric capsule may comprise a cylindrical body portion and a removable cylindrical lid portion. In such embodiments, the diameter of the removable cylindrical lid portion may be greater than the diameter of the cylindrical body portion so that the removable cylindrical lid portion fits over the cylindrical body portion.

The cylindrical polymeric capsule may have any suitable size.

The cylindrical polymeric capsule may have a length of, for example, between about 4 mm and about 12 mm. In certain preferred embodiments, the cylindrical polymeric capsule has a length of about 8 mm.

5 The cylindrical polymeric capsule may have a diameter of, for example, between about 4 mm and about 10 mm. In certain preferred embodiments, the cylindrical polymeric capsule has a diameter of about 7 mm.

The cylindrical polymeric capsule may have a thickness of, for example, between about 0.1 mm and about 1.0 mm. In certain preferred embodiments, the cylindrical polymeric capsule has a thickness of between about 0.2 mm and about 0.4 mm.

10 Where the nicotine source is encapsulated in a cylindrical polymeric capsule, the size of the cylindrical polymeric capsule in which the nicotine source is encapsulated may be chosen to allow a desired amount of nicotine to be included in the nicotine source.

15 Where the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule, the size of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may be chosen to allow a desired amount of volatile delivery enhancing compound to be included in the volatile delivery enhancing compound source.

20 Where the nicotine source and the volatile delivery enhancing compound source are both encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule in which the nicotine source is encapsulated and the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may be of the same or different sizes.

25 The cylindrical polymeric capsule may be formed from one or more suitable polymeric materials. Suitable polymeric materials include, but are not limited to, gelatin, polyethylene (PE), polypropylene (PP), polyurethane (PU), fluorinated ethylene propylene (FEP) and combinations thereof.

30 In certain preferred embodiments, the cylindrical polymeric capsule may be formed from one or more biodegradable polymeric materials. This may advantageously reduce the environmental impact of aerosol-generating systems according to the invention. Suitable biodegradable polymeric materials include, but are not limited to, polylactic acid (PLA) and polyhydroxybutyrate (PHB), cellulose acetate, poly-epsilon-caprolactone (PCL), polyglycolic acid (PGA), polyhydroxyalkanoates (PHAs) and starch-based thermoplastics.

35 Where the nicotine source and the volatile delivery enhancing compound source are both encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule in which the nicotine source is encapsulated and the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may be formed from the same or different polymeric materials.

Where the nicotine source is encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule in which the nicotine source is encapsulated may be formed from one or more nicotine-resistant polymeric materials.

Alternatively or in addition, where the nicotine source is encapsulated in a cylindrical polymeric capsule, the interior of the cylindrical polymeric capsule in which the nicotine source is encapsulated may be coated with one or more nicotine-resistant polymeric materials.

In such embodiments, the nicotine-resistant polymeric coating on the interior of the cylindrical polymeric capsule in which the nicotine source is encapsulated may have a thickness of, for example, between about 5 μm and about 100 μm . In certain preferred embodiments, the nicotine-resistant polymeric coating on the interior of the cylindrical polymeric capsule in which the nicotine source is encapsulated has a thickness of about 40 μm .

Examples of suitable nicotine-resistant polymeric materials include, but are not limited to, polyethylene (PE), polypropylene (PP), polystyrene (PS), fluorinated ethylene propylene (FEP), polytetrafluoroethylene (PTFE), epoxy resins, polyurethane resins, vinyl resins and combinations thereof.

Use of one or more nicotine-resistant polymeric materials to form or coat the interior of the cylindrical polymeric capsule in which the nicotine source is encapsulated may advantageously enhance the shelf life of aerosol-generating systems according to the invention.

Where the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule, the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may be formed from one or more volatile delivery enhancing compound-resistant polymeric materials.

Alternatively or in addition, where the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule, the interior of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may be coated with one or more volatile delivery enhancing compound-resistant polymeric materials.

In such embodiments, the volatile delivery enhancing compound-resistant polymeric coating on the interior of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may have a thickness of, for example, between about 5 μm and about 100 μm . In certain preferred embodiments, the volatile delivery enhancing compound -resistant polymeric coating on the interior of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated has a thickness of about 40 μm .

Examples of suitable volatile delivery enhancing compound-resistant polymeric materials include, but are not limited to, polyethylene (PE), polypropylene (PP), polystyrene (PS), fluorinated ethylene propylene (FEP), polytetrafluoroethylene (PTFE), epoxy resins, polyurethane resins, vinyl resins and combinations thereof.

Use of one or more volatile delivery enhancing compound-resistant polymeric materials to form or coat the interior of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated may advantageously enhance the shelf life of aerosol-generating systems according to the invention.

5 Aerosol-generating systems according to the invention comprise heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source. As described further below, inclusion of a thermally conductive material in the cylindrical polymeric capsule advantageously facilitates heating of the nicotine source or the volatile delivery enhancing compound source encapsulated in the cylindrical polymeric capsule
10 by the heating means.

The thermally conductive material may be included in one or more walls of the cylindrical polymeric capsule.

In such embodiments the thermally conductive material may be included in one or both of the opposed substantially planar end faces of the cylindrical polymeric capsule. Alternatively
15 or in addition, in such embodiments the thermally conductive material may be included in the circumferential wall of the cylindrical polymeric capsule.

Alternatively or in addition, the thermally conductive material may be included in a polymeric coating provided on at least a portion of the interior surface of the cylindrical polymeric capsule.

20 In such embodiments the thermally conductive material may be included in a polymeric coating provided on the interior surface of one or both of the opposed substantially planar end faces of the cylindrical polymeric capsule. Alternatively or in addition, in such embodiments the thermally conductive material may be included in a polymeric coating provided on the interior surface of the circumferential wall of the cylindrical polymeric capsule.

25 In preferred embodiments, the thermally conductive material is included in the circumferential wall of the cylindrical polymeric capsule or in a polymeric coating provided on the interior surface of the circumferential wall of the cylindrical polymeric capsule.

In particularly preferred embodiments, the thermally conductive material is included in the opposed substantially planar end faces and the circumferential wall of the cylindrical
30 polymeric capsule or in a polymeric coating provided on the interior surface of the opposed substantially planar end faces and the circumferential wall of the cylindrical polymeric capsule.

Preferably, the thermally conductive material is substantially homogeneously distributed within the capsule.

The thermally conductive material may be incorporated in one or more polymeric
35 materials used to form the cylindrical polymeric capsule. Alternatively or in addition, a thermally conductive material may be incorporated in one or more polymeric materials used to form a polymeric coating on the interior of the cylindrical polymeric capsule. Inclusion of a thermally

conductive material in one or both of one or more polymeric materials used to form the cylindrical polymeric capsule or one or more polymeric materials used to coat the interior of the cylindrical polymeric capsule advantageously increases heat transfer to the nicotine source or the volatile delivery enhancing compound source encapsulated in the cylindrical polymeric capsule.

Preferably, the thermally conductive material has a thermal conductivity of at least about 10 W per metre ($W/(m \cdot K)$), more preferably at least about 50 W per metre Kelvin ($W/(m \cdot K)$), most preferably at least about 100 W per metre Kelvin ($W/(m \cdot K)$) at 23°C and a relative humidity of 50% as measured using the modified transient plane source (MTPS) method.

Suitable thermally conductive materials include, but are not limited to, metals such as, for example, aluminium, chromium, copper, gold, iron, nickel and silver, alloys, such as brass and steel, and combinations thereof and non-metallic materials such as, for example, diamond, boron carbide (BC), graphite, silicon carbide (SiC), beryllium oxide (BeO), beryllium sulfide (BeS), aluminium nitride (AlN), boron phosphide (BP) and thermally conductive polymers such as, for example, ultra high molecular weight polyethylene (UHMWPE).

A thermally conductive material may be incorporated in one or both of the cylindrical polymeric capsule and a polymeric coating on the interior of the cylindrical polymeric capsule by any suitable method. For example, a plurality of particles of thermally conductive material may be mixed into: one or more polymeric materials used to form the cylindrical polymeric capsule prior to formation of the cylindrical polymeric capsule; or one or more polymeric materials used to form a polymeric coating on the interior of the cylindrical polymeric capsule prior to application of the coating.

In certain preferred embodiments, at least a portion of the cylindrical polymeric capsule has a plurality of particles of thermally conductive material embedded therein.

In certain particularly preferred embodiments, at least a portion of the cylindrical polymeric capsule has a plurality of metal particles embedded therein.

In other preferred embodiments, at least a portion of the interior of the cylindrical polymeric capsule is coated with a polymeric coating comprising a plurality of particles of thermally conductive material.

In other particularly preferred embodiments, at least a portion of the interior of the cylindrical polymeric capsule is coated with a polymeric coating comprising a plurality of metal particles.

Cylindrical polymeric capsules for use in aerosol-generating systems according to the invention may be formed by any suitable method. Suitable methods include, but are not limited to, dipping, blowing, blow moulding and injection moulding.

In particularly preferred embodiments, cylindrical polymeric capsules for use in aerosol-generating systems according to the invention are formed by dipping using cylindrical dipping

bars. This advantageously enables the cylindrical polymeric capsules to be mass-produced in a high-speed and cost-effective manner.

Preferably, aerosol-generating systems according to the invention further comprise a piercing member for piercing the cylindrical polymeric capsule. More preferably, aerosol-generating systems according to the invention further comprise a piercing member for piercing the opposed substantially planar end faces of the cylindrical polymeric capsule. In such embodiments, the shape of the cylindrical polymeric capsule advantageously facilitates piercing of the cylindrical polymeric capsule by the piercing member.

Where the nicotine source and the volatile delivery enhancing compound source are both encapsulated in a cylindrical polymeric capsule, aerosol-generating systems according to the invention preferably further comprise a piercing member for piercing both the cylindrical polymeric capsule in which the nicotine source is encapsulated and the cylindrical polymeric capsule in which the volatile delivery enhancing compound is encapsulated.

The piercing member may be formed from any suitable material.

To further facilitate piercing of the cylindrical polymeric capsule by the piercing member, the cylindrical polymeric capsule may comprise one or more regions of reduced strength.

Preferably, one or both of the opposed planar end faces of the cylindrical polymeric capsule are provided with a region of reduced strength. More preferably, both of the opposed planar end faces of the cylindrical polymeric capsule are provided with a region of reduced strength.

The provision of one or more regions of reduced strength advantageously allows the piercing member to pierce the cylindrical polymeric capsule in a controlled and repeatable manner.

The one or more regions of reduced strength may be formed by any suitable method. Suitable methods include, but are not limited to, laser etching, chemical etching and mechanical piercing.

Aerosol-generating systems according to the invention comprise heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source.

Heating one or both of the nicotine source and the volatile delivery enhancing compound source to a temperature above ambient temperature allows control of the amount of nicotine vapour and volatile delivery enhancing compound vapour released from the nicotine source and the volatile delivery enhancing compound source, respectively. This advantageously enables the vapour concentrations of the nicotine and the volatile delivery enhancing compound to be controlled and balanced proportionally to yield an efficient reaction stoichiometry. This advantageously improves the efficiency of the formation of an aerosol and the consistency of

nicotine delivery to a user. It also advantageously reduces the delivery of unreacted nicotine vapour and unreacted volatile delivery enhancing compound vapour to a user.

In certain preferred embodiments, the aerosol-generating system comprises heating means configured to heat one or both of the nicotine source and the volatile delivery enhancing compound source to a temperature of between about 60 degrees Celsius and about 150 degrees Celsius. More, preferably to a temperature of between about 80 degrees Celsius and about 150 degrees Celsius.

In certain preferred embodiments, the aerosol-generating system comprises heating means for heating the nicotine source.

The heating means may comprise an external heater.

As used herein, the term "external heater" refers to a heater that in use is positioned externally to the nicotine source and the volatile delivery enhancing compound source of aerosol-generating systems according to the invention.

The heating means may comprise an external heater disposed about the circumference of one or both of the nicotine source and the volatile delivery enhancing compound source.

In certain embodiments, the heating means may comprise an external heater disposed about the circumference of both the nicotine source and the volatile delivery enhancing compound source.

Alternatively or in addition, the heating means may comprise an internal heater.

As used herein, the term "internal heater" refers to a heater that in use is positioned internally to one or both of the nicotine source and volatile delivery enhancing compound source of aerosol-generating systems according to the invention.

The heating means may be an electric heating means.

Where the heating means is an electric heating means, the aerosol-generating system may further comprise an electric power supply. Alternatively, the electric heating means may be powered by an external electric power supply.

Where the heating means is an electric heating means, the aerosol-generating system may also further comprise electronic circuitry configured to control the supply of electric power from the electric power supply to the electric heating means. Any suitable electronic circuitry may be used in order to control the supply of power to the electric heating means. The electronic circuitry may be programmable.

The electric power supply may be a DC voltage source. In certain embodiments, the electric power supply is a battery. For example, the electric power supply may be a Nickel-metal hydride battery, a Nickel cadmium battery, or a Lithium based battery, for example a Lithium-Cobalt, a Lithium-Iron-Phosphate or a Lithium-Polymer battery. The electric power supply may alternatively be another form of electric charge storage device such as a capacitor. The electric power supply may be rechargeable.

Alternatively, the heating means may be powered by a non-electric power supply, such as a combustible fuel. For example, the heating means may comprise a thermally conductive element that is heated by combustion of a gaseous fuel.

Alternatively, the heating means may be a non-electric heating means, such as a chemical heating means.

In certain embodiments the heating means may comprise a heat sink or heat exchanger configured to transfer thermal energy from an external heat source to one or both of the nicotine source and the volatile delivery enhancing compound source. The heat sink or heat exchanger may be formed of any suitable thermally conductive material. Suitable thermally conductive materials include, but are not limited to, metals, such as aluminium and copper.

In certain particularly preferred embodiments, the aerosol-generating system comprises: a nicotine source; a volatile delivery enhancing compound source; heating means for heating the nicotine source; and a heat transfer barrier between the nicotine source and the delivery enhancing compound source, wherein one or both of the nicotine source and the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule and wherein the cylindrical polymeric capsule comprises a thermally conductive material.

In such embodiments, the heat transfer barrier separates the nicotine source and the volatile delivery enhancing compound source and is configured to reduce heat transfer between the nicotine source and the volatile delivery enhancing compound source.

Inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source advantageously enables the volatile delivery enhancing compound source to be maintained at a lower temperature while the nicotine source is heated to a higher temperature. In particular, inclusion of a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source advantageously enables the nicotine delivery of the aerosol-generating system to be significantly increased by increasing the temperature of the nicotine source while the volatile delivery enhancing compound source is maintained at a temperature below the thermal decomposition temperature of the volatile delivery enhancing compound.

Differential heating of the nicotine source and the volatile delivery enhancing compound source advantageously enables the vapour concentrations of the nicotine and the volatile delivery enhancing compound to be controlled and balanced proportionally to yield an efficient reaction stoichiometry. This advantageously improves the efficiency of the formation of an aerosol and the consistency of nicotine delivery to a user.

As used herein, the term "heat transfer barrier" is used to describe a physical barrier that reduces the amount of heat transferred from the nicotine source to the volatile delivery enhancing compound source compared to an aerosol-generating system in which no barrier is present.

The physical barrier may comprise a solid material. For example, in certain embodiments the heat transfer barrier may comprise a solid material having a thermal conductivity of less than about 1W per metre Kelvin ($W/(m \cdot K)$) at 23°C and a relative humidity of 50% as measured using the modified transient plane source (MTPS) method. Alternatively or in addition, the physical barrier may comprise a gas, vacuum or partial vacuum between the nicotine source and the volatile delivery enhancing compound source. For example, in certain embodiments the heat transfer barrier may comprise a cavity having a length of at least about 8 mm.

Where aerosol-generating systems according to the invention comprise a heat transfer barrier between the nicotine source and the volatile delivery enhancing compound source, the heating means is preferably configured to heat the nicotine source to a temperature of between about 80°C and about 150°C. In such embodiments, the heat transfer barrier is preferably configured so that in use the temperature of the volatile delivery enhancing compound source is below about 60°C when the nicotine source is heated to a temperature of between 80°C and 150°C.

Aerosol-generating systems according to the invention comprise a volatile delivery enhancing compound source. As used herein, by “volatile” it is meant the delivery enhancing compound has a vapour pressure of at least about 20 Pa. Unless otherwise stated, all vapour pressures referred to herein are vapour pressures at 25°C measured in accordance with ASTM E1194 – 07.

Preferably, the volatile delivery enhancing compound has a vapour pressure of at least about 50 Pa, more preferably at least about 75 Pa, most preferably at least 100 Pa at 25°C.

Preferably, the volatile delivery enhancing compound has a vapour pressure of less than or equal to about 400 Pa, more preferably less than or equal to about 300 Pa, even more preferably less than or equal to about 275 Pa, most preferably less than or equal to about 250 Pa at 25°C.

In certain embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 20 Pa and about 400 Pa, more preferably between about 20 Pa and about 300 Pa, even more preferably between about 20 Pa and about 275 Pa, most preferably between about 20 Pa and about 250 Pa at 25°C.

In other embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 50 Pa and about 400 Pa, more preferably between about 50 Pa and about 300 Pa, even more preferably between about 50 Pa and about 275 Pa, most preferably between about 50 Pa and about 250 Pa at 25°C.

In further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 75 Pa and about 400 Pa, more preferably between about 75 Pa and

about 300 Pa, even more preferably between about 75 Pa and about 275 Pa, most preferably between about 75 Pa and about 250 Pa at 25°C.

In yet further embodiments, the volatile delivery enhancing compound may have a vapour pressure of between about 100 Pa and about 400 Pa, more preferably between about 100 Pa and about 300 Pa, even more preferably between about 100 Pa and about 275 Pa, most preferably between about 100 Pa and about 250 Pa at 25°C.

The volatile delivery enhancing compound may comprise a single compound. Alternatively, the volatile delivery enhancing compound may comprise two or more different compounds.

Where the volatile delivery enhancing compound comprises two or more different compounds, the two or more different compounds in combination preferably have a vapour pressure of at least about 20 Pa at 25°C.

Preferably, the volatile delivery enhancing compound is a volatile liquid.

The volatile delivery enhancing compound may comprise a mixture of two or more different liquid compounds.

The volatile delivery enhancing compound may comprise an aqueous solution of one or more compounds. Alternatively the volatile delivery enhancing compound may comprise a non-aqueous solution of one or more compounds.

The volatile delivery enhancing compound may comprise two or more different volatile compounds. For example, the volatile delivery enhancing compound may comprise a mixture of two or more different volatile liquid compounds.

Alternatively, the volatile delivery enhancing compound may comprise one or more non-volatile compounds and one or more volatile compounds. For example, the volatile delivery enhancing compound may comprise a solution of one or more non-volatile compounds in a volatile solvent or a mixture of one or more non-volatile liquid compounds and one or more volatile liquid compounds.

The volatile delivery enhancing compound comprises an acid. The volatile delivery enhancing compound may comprise an organic acid or an inorganic acid. Preferably, the volatile delivery enhancing compound comprises an organic acid, more preferably a carboxylic acid, most preferably lactic acid or an alpha-keto or 2-oxo acid.

In certain preferred embodiments, the volatile delivery enhancing compound comprises an acid selected from the group consisting of lactic acid, 3-methyl-2-oxopentanoic acid, pyruvic acid, 2-oxopentanoic acid, 4-methyl-2-oxopentanoic acid, 3-methyl-2-oxobutanoic acid, 2-oxooctanoic acid and combinations thereof. In certain particularly preferred embodiments, the volatile delivery enhancing compound comprises lactic acid or pyruvic acid.

In certain embodiments, the volatile delivery enhancing compound source comprises a sorption element and a volatile delivery enhancing compound sorbed on the sorption element.

As used herein, by "sorbed" it is meant that the volatile delivery enhancing compound is adsorbed on the surface of the sorption element, or absorbed in the sorption element, or both adsorbed on and absorbed in the sorption element. Preferably, the volatile delivery enhancing compound is adsorbed on the sorption element.

5 The sorption element may be formed from any suitable material or combination of materials. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and BAREX®.

10 In certain preferred embodiments, the sorption element is a porous sorption element. For example, the sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

The sorption element is preferably chemically inert with respect to the volatile delivery enhancing compound.

The sorption element may have any suitable size and shape.

In certain preferred embodiments, the sorption element is a substantially cylindrical plug. In certain particularly preferred embodiments, the sorption element is a porous substantially cylindrical plug.

20 In other preferred embodiments, the sorption element is a substantially cylindrical hollow tube. In other particularly preferred embodiments, the sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the sorption element may be chosen to allow a desired amount of volatile delivery enhancing compound to be sorbed on the sorption element.

25 In certain preferred embodiments, between about 20 µl and about 200 µl, more preferably between about 40 µl and about 150 µl, most preferably between about 50 µl and about 100 µl of the volatile delivery enhancing compound is sorbed on the sorption element.

The sorption element advantageously acts as a reservoir for the volatile delivery enhancing compound.

30 The nicotine source may comprise one or more of nicotine, nicotine base, a nicotine salt, such as nicotine-HCl, nicotine-bitartrate, or nicotine-ditartrate, or a nicotine derivative.

The nicotine source may comprise natural nicotine or synthetic nicotine.

The nicotine source may comprise pure nicotine, a solution of nicotine in an aqueous or non-aqueous solvent or a liquid tobacco extract.

35 The nicotine source may further comprise an electrolyte forming compound. The electrolyte forming compound may be selected from the group consisting of alkali metal

hydroxides, alkali metal oxides, alkali metal salts, alkaline earth metal oxides, alkaline earth metal hydroxides and combinations thereof.

For example, the nicotine source may comprise an electrolyte forming compound selected from the group consisting of potassium hydroxide, sodium hydroxide, lithium oxide, barium oxide, potassium chloride, sodium chloride, sodium carbonate, sodium citrate, ammonium sulfate and combinations thereof

In certain embodiments, the nicotine source may comprise an aqueous solution of nicotine, nicotine base, a nicotine salt or a nicotine derivative and an electrolyte forming compound.

Alternatively or in addition, the nicotine source may further comprise other components including, but not limited to, natural flavours, artificial flavours and antioxidants.

The nicotine source may comprise a sorption element and nicotine sorbed on the sorption element.

The sorption element may be formed from any suitable material or combination of materials. For example, the sorption element may comprise one or more of glass, stainless steel, aluminium, polyethylene (PE), polypropylene, polyethylene terephthalate (PET), polybutylene terephthalate (PBT), polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene (ePTFE), and BAREX®.

In certain preferred embodiments, the sorption element is a porous sorption element. For example, the sorption element may be a porous sorption element comprising one or more materials selected from the group consisting of porous plastic materials, porous polymer fibres and porous glass fibres.

The sorption element is preferably chemically inert with respect to nicotine.

The sorption element may have any suitable size and shape.

In certain preferred embodiments, the sorption element is a substantially cylindrical plug. In certain particularly preferred embodiments, the sorption element is a porous substantially cylindrical plug.

In other preferred embodiments, the sorption element is a substantially cylindrical hollow tube. In other particularly preferred embodiments, the sorption element is a porous substantially cylindrical hollow tube.

The size, shape and composition of the sorption element may be chosen to allow a desired amount of nicotine to be sorbed on the sorption element.

The sorption element advantageously acts as a reservoir for the nicotine.

Aerosol-generating systems according to the invention may comprise a first compartment comprising the nicotine source and a second compartment comprising the volatile delivery enhancing compound source.

As used herein, the term "compartment" is used to describe a chamber or container within the aerosol-generating system comprising the nicotine source or the volatile delivery enhancing compound source.

5 The first compartment may comprise or consist of the nicotine source encapsulated in a cylindrical polymeric capsule.

The second compartment may comprise or consist of the volatile delivery enhancing compound source encapsulated in a cylindrical polymeric capsule.

10 The first compartment and the second compartment of the aerosol-generating system may abut one another. Alternatively, the first compartment and the second compartment of the aerosol-generating system may be spaced apart from one another.

The volume of the first compartment and the second compartment may be the same or different. In certain preferred embodiment, the volume of the first compartment is greater than the volume of the second compartment.

15 As described further below, the first compartment and the second compartment may be arranged in series or parallel within the aerosol-generating system.

As used herein, by "series" it is meant that the first compartment and the second compartment are arranged within the aerosol-generating system so that in use an air stream drawn through the aerosol-generating system passes through one of the first compartment and the second compartment and then passes through the other of the first compartment and the second compartment. Nicotine vapour is released from the nicotine source in the first compartment into the air stream drawn through the aerosol-generating system and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment into the air stream drawn through the aerosol-generating system. The nicotine vapour reacts with the volatile delivery enhancing compound vapour in the gas phase to form an aerosol, which is delivered to a user.

20
25

Where the first compartment and the second compartment are arranged in series within the aerosol-generating system, the second compartment is preferably downstream of the first compartment so that in use an air stream drawn through the aerosol-generating article passes through the first compartment and then passes through the second compartment.

30 Location of the second compartment comprising the volatile delivery enhancing compound source downstream of the first compartment comprising the nicotine source advantageously improves the consistency of the nicotine delivery of aerosol-generating systems according to the invention.

Without being bound by theory, it is believed that location of the volatile delivery enhancing compound source downstream of the nicotine source reduces or prevents deposition of volatile delivery enhancing compound vapour released from the volatile delivery enhancing

35

compound source on the nicotine source during use. This reduces fading over time of the nicotine delivery in aerosol-generating systems according to the invention.

In such embodiments, the nicotine vapour may react with the volatile delivery enhancing compound vapour in the second compartment to form an aerosol. In such embodiments the aerosol-generating system may further comprise a third compartment downstream of the second compartment and the nicotine vapour may alternatively or in addition react with the volatile delivery enhancing compound vapour in the third compartment to form an aerosol.

As used herein, by "parallel" it is meant that the first compartment and the second compartment are arranged within the aerosol-generating system so that in use a first air stream drawn through the aerosol-generating system passes through the first compartment and a second air stream drawn through the aerosol-generating system passes through the second compartment. Nicotine vapour is released from the nicotine source in the first compartment into the first air stream drawn through the aerosol-generating system and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment into the second air stream drawn through the aerosol-generating system. The nicotine vapour in the first air stream reacts with the volatile delivery enhancing compound vapour in the second air stream in the gas phase to form an aerosol, which is delivered to a user.

In such embodiments the aerosol-generating system may further comprise a third compartment downstream of the first compartment and the second compartment and the nicotine vapour in the first air stream may mix and react with the volatile delivery enhancing compound vapour in the second air stream in the third compartment to form an aerosol.

In certain particularly preferred embodiments, the aerosol-generating system comprises: a housing comprising: an air inlet; a first compartment in communication with the air inlet, the first compartment comprising a first one of the nicotine source and the volatile delivery enhancing compound source; a second compartment in communication with the first compartment, the second compartment comprising a second one of the nicotine source and the volatile delivery enhancing compound source; and an air outlet, wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

As used herein, the term "air inlet" is used to describe one or more apertures through which air may be drawn into the aerosol-generating system.

As used herein, the term "air outlet" is used to describe one or more apertures through which air may be drawn out of the aerosol-generating system.

In such embodiments, the first compartment and the second compartment are arranged in series from air inlet to air outlet within the housing. That is, the first compartment is downstream of the air inlet, the second compartment is downstream of the first compartment

and the air outlet is downstream of the second compartment. In use, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment and the second compartment and out of the housing through the air outlet.

In such embodiments, the first compartment preferably comprises the nicotine source
5 and the second compartment preferably comprises the volatile delivery enhancing source.

The aerosol-generating system may further comprise a third compartment in communication with: the second compartment; and the air outlet. In use in such embodiments, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment, the second compartment and the third compartment and out of the housing
10 through the air outlet.

The aerosol-generating system may further comprise a mouthpiece in communication with: the second compartment or the third compartment, where present; and the air outlet. In use in such embodiments, a stream of air is drawn into the housing through the air inlet, downstream through the first compartment, the second compartment, the third compartment,
15 where present, and the mouthpiece and out of the housing through the air outlet.

In other preferred embodiments, the aerosol-generating system comprises: a housing comprising: an air inlet; a first compartment in communication with the air inlet, the first compartment comprising the nicotine source; a second compartment in communication with the air inlet, the second compartment comprising the volatile delivery enhancing compound source;
20 and an air outlet, wherein the air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the air inlet, through the housing and out of the housing through the air outlet.

In such embodiments, the first compartment and the second compartment are arranged in parallel from air inlet to air outlet within the housing. The first compartment and the second
25 compartment are both downstream of the air inlet and upstream of the air outlet. In use, a stream of air is drawn into the housing through the air inlet, a first portion of the stream of air is drawn downstream through the first compartment and a second portion of the stream of air is drawn downstream through the second compartment.

The aerosol-generating system may further comprise a third compartment in communication with: one or both of the first compartment and the second compartment; and the
30 air outlet.

The aerosol-generating system may further comprise a mouthpiece in communication with: the first compartment and the second compartment, or the third compartment, where present; and the air outlet.

In further preferred embodiments, the aerosol-generating system comprises: a housing comprising: a first air inlet; a second air inlet; a first compartment in communication with the first
35 air inlet, the first compartment comprising the nicotine source; a second compartment in

communication with the second air inlet, the second compartment comprising the volatile delivery enhancing compound source; and an air outlet, wherein the first air inlet, the second air inlet and the air outlet are in communication with each other and configured so that air may pass into the housing through the first air inlet, through the housing and out of the housing through the air outlet and air may pass into the housing through the first air inlet, through the housing and out of the housing through the air outlet.

In such embodiments, the first compartment and the second compartment are arranged in parallel within the housing. The first compartment is downstream of the first air inlet and upstream of the air outlet and the second compartment is downstream of the second air inlet and upstream of the air outlet. In use, a first stream of air is drawn into the housing through the first air inlet and downstream through the first compartment and a second stream of air is drawn into the housing through the second air inlet and downstream through the second compartment.

The aerosol-generating system may further comprise a third compartment in communication with: one or both of the first compartment and the second compartment; and the air outlet.

The aerosol-generating system may further comprise a mouthpiece in communication with: the first compartment and the second compartment, or the third compartment, where present; and the air outlet.

Where aerosol-generating systems according to the invention comprise a housing, the housing may be designed to be grasped or held by a user.

Preferably, the housing is substantially cylindrical.

Where aerosol-generating systems according to the invention comprise a third compartment, the third compartment may comprise one or more aerosol-modifying agents. For example, the third compartment may comprise one or more sorbents, such as activated carbon, one or more flavourants, such as menthol, or a combination thereof.

Where aerosol-generating systems according to the invention comprise a mouthpiece, the mouthpiece may comprise a filter. The filter may have a low particulate filtration efficiency or very low particulate filtration efficiency. Alternatively, the mouthpiece may comprise a hollow tube.

In certain particularly preferred embodiments, aerosol-generating systems according to the invention comprise: an aerosol-generating article comprising the nicotine source and the volatile delivery enhancing compound source; and an aerosol-generating device configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article.

Preferably, the aerosol-generating article is substantially cylindrical. The aerosol-generating article may simulate the shape and dimensions of a tobacco smoking article, such as

a cigarette, a cigar, a cigarillo or a pipe, or a cigarette pack. In certain preferred embodiments, the aerosol-generating article simulates the shape and dimensions of a cigarette.

The aerosol-generating device preferably comprises a cavity configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article.

Preferably, the cavity of the aerosol-generating device is substantially cylindrical.

Preferably, the cavity of the aerosol-generating device has a diameter substantially equal to or slightly greater than the diameter of the aerosol-generating article.

Preferably, the length of the cavity of the aerosol-generating device is less than the length of the aerosol-generating article so that when the aerosol-generating article is received in the cavity of the aerosol-generating device the proximal or downstream end of the aerosol-generating article projects from the cavity of the aerosol-generating device.

The aerosol-generating device preferably comprises heating means as described above for heating one or both of the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article.

Where the aerosol-generating device comprises a cavity configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article, the heating means may comprise an external heater positioned about a perimeter of the cavity. Alternatively, the heating means may comprise an internal heater positioned within the cavity.

The aerosol-generating device preferably comprises a piercing member as described above for piercing the cylindrical polymeric capsule.

The aerosol-generating article may comprise a first compartment comprising the nicotine source and a second compartment comprising the volatile delivery enhancing compound source as described above. As previously described, the first compartment and the second compartment may be arranged in series or parallel within the aerosol-generating article.

Where the first compartment and the second compartment are arranged in series within the aerosol-generating article, the aerosol-generating device may comprise a piercing member positioned centrally within the cavity of the aerosol-generating device, along the major axis of the cavity, for piercing the first compartment and the second compartment of the aerosol-generating article.

Where the first compartment and the second compartment of the aerosol-generating article are arranged in parallel within the aerosol-generating article, the aerosol-generating device may further comprise a piercing member comprising a first piercing member positioned within the cavity of the aerosol-generating device for piercing the first compartment of the aerosol-generating article and a second piercing member positioned within the cavity of the aerosol-generating device for piercing the second compartment of the aerosol-generating

article.

For the avoidance of doubt, features described above in relation to one aspect of the invention may also be applicable to other aspects of the invention. In particular, features described above in relation to aerosol-generating systems according to the invention may also relate, where appropriate, to one or both of aerosol-generating articles and aerosol-generating devices of aerosol-generating systems according to the invention, and vice versa.

All scientific and technical terms used herein have meanings commonly used in the art unless otherwise specified. The definitions provided herein are to facilitate understanding of certain terms used frequently herein.

As used herein, the singular forms “a”, “an”, and “the” encompass embodiments having plural referents, unless the context clearly dictates otherwise.

The words “preferred” and “preferably” refer to embodiments of the invention that may afford certain benefits, under certain circumstances. Particularly preferred are aerosol-generating systems according to the invention comprising combinations of preferred features. However, it will be appreciated that other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the claims.

The invention will now be further described with reference to the accompanying drawings in which:

Figure 1 shows a schematic drawing of a cylindrical polymeric capsule for use in an aerosol-generating system according to the invention; and

Figure 2 shows a schematic longitudinal cross-section of an aerosol-generating system according to an embodiment of the invention comprising: an aerosol-generating article comprising a nicotine source and a volatile delivery enhancing compound source; and an aerosol-generating device configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article.

The cylindrical polymeric capsule 2 shown in Figure 1 comprises a cylindrical body portion 2a and a removable cylindrical lid portion 2b. A plurality of metal particles (not shown) are embedded in the cylindrical body portion 2a and the removable cylindrical lid portion 2b of the cylindrical polymeric capsule 2. The metal particles are preferably substantially homogeneously distributed in the capsule.

The aerosol-generating system shown in Figure 2 comprises an aerosol-generating article 4 and an aerosol-generating device 6.

The aerosol-generating article 4 has an elongate cylindrical shape and comprises a housing comprising: a first compartment 8 consisting of a nicotine source encapsulated in a cylindrical polymeric capsule 2 of the type shown in Figure 1; a second compartment 10

consisting of a volatile delivery enhancing compound source encapsulated in a cylindrical polymeric capsule 2 of the type shown in Figure 1; a third compartment 12; and a mouthpiece 14.

The first compartment 8, the second compartment 10, the third compartment 12 and the mouthpiece 14 are arranged in series and in coaxial alignment within the aerosol-generating article 4. The first compartment 8 is located at the distal end of the aerosol-generating article 4. The second compartment 10 is located immediately downstream of the first compartment 8. The third compartment 12 is located immediately downstream of the second compartment 10. The mouthpiece 14 is located immediately downstream of the third compartment 12 at the proximal end of the aerosol-generating article 4.

A heat transfer barrier (not shown) may be provided between the first compartment 8 and the second compartment 10 to reduce heat transfer between the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article 4.

The aerosol-generating device 6 comprises a housing comprising an elongate cylindrical cavity in which the aerosol-generating article 4 is received. As shown in Figure 2, the length of the cavity is less than the length of the aerosol-generating article 4 so that when the aerosol-generating article 4 is inserted into the aerosol-generating device 6 the proximal end of the aerosol-generating article 4 protrudes from the cavity.

The aerosol-generating device 6 further comprises a power supply 16, a controller (not shown), heating means 18, and a piercing element 20. The power supply 16 is a battery and the controller comprises electronic circuitry and is connected to the power supply 16 and the heating means 18.

The heating means 18 comprises an external heating element positioned about the perimeter of a portion of the cavity at the distal end thereof and extends fully around the circumference of the cavity. As shown in Figure 2, the external heating element is positioned so that it circumscribes the first compartment 8 of the aerosol-generating article 4.

The piercing element 20 is positioned centrally within the cavity of the aerosol-generating device 6 and extends along the major axis of the cavity.

In use, as the aerosol-generating article 4 is inserted into the cavity of the aerosol-generating device 6 the piercing member 20 of the aerosol-generating device 6 is inserted into the aerosol-generating article 4 and pierces the cylindrical polymeric capsule 2 of the first compartment 8 in which the nicotine source is encapsulated and the cylindrical polymeric capsule 2 of the second compartment 10 in which the volatile delivery enhancing compound source is encapsulated. This allows a user to draw air into the housing of the aerosol-generating article 4 through the distal or upstream end thereof, downstream through the first compartment 8, the second compartment 10 and the third compartment 12 and out of the housing through the mouthpiece 14 at the proximal end thereof.

As the user draws air through the aerosol-generating article 4, nicotine vapour is released from the nicotine source in the first compartment 8 into the air stream drawn through the aerosol-generating article 4 and volatile delivery enhancing compound vapour is released from the volatile delivery enhancing compound source in the second compartment 10 into the air stream drawn through the aerosol-generating article 4. The nicotine vapour reacts with the volatile delivery enhancing compound vapour in the gas phase in the second compartment 10 and the third compartment 12 to form an aerosol, which is delivered to the user through the mouthpiece 14 at the proximal end of the aerosol-generating article 4.

The external heating element of the heating means 18 heats the first compartment 6 of the aerosol-generating article 4 received in the cavity of the aerosol-generating device 6. The plurality of metals particles embedded in the cylindrical body portion 2a and the removable cylindrical lid portion 2b of the cylindrical polymeric capsule 2 increase heat transfer to the nicotine source encapsulated in the cylindrical polymeric capsule 2 and so facilitate heating of the nicotine source by the external heating element of the heating means 18.

In an alternative embodiment of the invention (not shown), the external heating element heating means 18 is positioned so that it circumscribes the first compartment 8 and the second compartment 10 of the aerosol-generating article 4. In this alternative embodiment, the external heating element of the heating means 18 heats the first compartment 6 and the second compartment 10 of the aerosol-generating article 4 received in the cavity of the aerosol-generating device 6.

The invention has been exemplified above by reference to an aerosol-generating system comprising a nicotine source and a volatile delivery enhancing compound source, wherein both the nicotine source and the volatile delivery enhancing compound source are encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material. However, it will be appreciated that in other embodiments only one of the nicotine source and the volatile delivery enhancing compound source of aerosol-generating systems according to the invention may be encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material.

For example, in other embodiments one of the nicotine source and the volatile delivery enhancing compound source may be encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material and the other of the nicotine source and the volatile delivery enhancing compound source may be encapsulated in a cylindrical polymeric capsule that does not comprise a thermally conductive material.

The invention has also been exemplified above by reference to an aerosol-generating system comprising an aerosol-generating article comprising a nicotine source and a volatile delivery enhancing compound source arranged in series within the aerosol-generating article. However, it will be appreciated that in other embodiments the nicotine source and the volatile

delivery enhancing compound source of aerosol-generating systems according to the invention may be arranged in parallel.

CLAIMS:

1. An aerosol-generating system comprising:
a nicotine source;
5 a volatile delivery enhancing compound source, wherein the volatile delivery enhancing compound comprises an acid; and
a heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source,
wherein one or both of the nicotine source and the volatile delivery enhancing compound
10 source is encapsulated in a cylindrical polymeric capsule comprising a thermally conductive material.
2. An aerosol-generating system according to claim 1 wherein the thermally conductive material has a thermal conductivity of at least about 10 W/(m•K).
- 15 3. An aerosol-generating system according to claim 1 or 2 wherein the thermally conductive material is included in one or more walls of the cylindrical polymeric capsule.
4. An aerosol-generating system according to any one of claims 1 to 3 wherein the
20 thermally conductive material is included in a polymeric coating provided on at least part of the interior surface of the cylindrical polymeric capsule.
5. An aerosol-generating system according to claim 1 wherein the thermally conductive material is substantially homogeneously distributed within the capsule.
- 25 6. An aerosol-generating system according to any one of claims 1 to 5 wherein the nicotine source is encapsulated in a cylindrical polymeric capsule.
7. An aerosol-generating system according to claim 6 wherein the interior of the cylindrical
30 polymeric capsule in which the nicotine source is encapsulated is coated with one or more nicotine-resistant polymeric materials.
8. An aerosol-generating system according to any one of claims 1 to 7 wherein the volatile delivery enhancing compound source is encapsulated in a cylindrical polymeric capsule.
- 35

9. An aerosol-generating system according to claim 8 wherein the interior of the cylindrical polymeric capsule in which the volatile delivery enhancing compound source is encapsulated is coated with one or more volatile delivery enhancing compound-resistant polymeric materials.
- 5 10. An aerosol-generating system according to any one of claims 1 to 9 further comprising:
a piercing member for piercing the cylindrical polymeric capsule.
11. An aerosol-generating system according to claim 10 wherein the cylindrical polymeric capsule comprises one or more regions of reduced strength to facilitate piercing of the
10 cylindrical polymeric capsule by the piercing member.
12. An aerosol-generating system according to claim 11 wherein the one or more regions of reduced strength are formed by laser etching.
- 15 13. An aerosol-generating system according to any one of claims 1 to 12 comprising:
an aerosol-generating article comprising the nicotine source and the volatile delivery enhancing compound source; and
an aerosol-generating device configured to receive the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article, wherein the aerosol-
20 generating device comprises heating means for heating one or both of the nicotine source and the volatile delivery enhancing compound source of the aerosol-generating article.
14. An aerosol-generating system according to claim 13 wherein the aerosol-generating device comprises a piercing member for piercing the cylindrical polymeric capsule.
25
15. An aerosol-generating article for use in an aerosol-generating system according to claim 13 or 14.
16. Use of a cylindrical polymeric capsule comprising a thermally conductive material in an
30 aerosol-generating system for generating a nicotine-containing aerosol comprising a heating means.

- 1/1 -

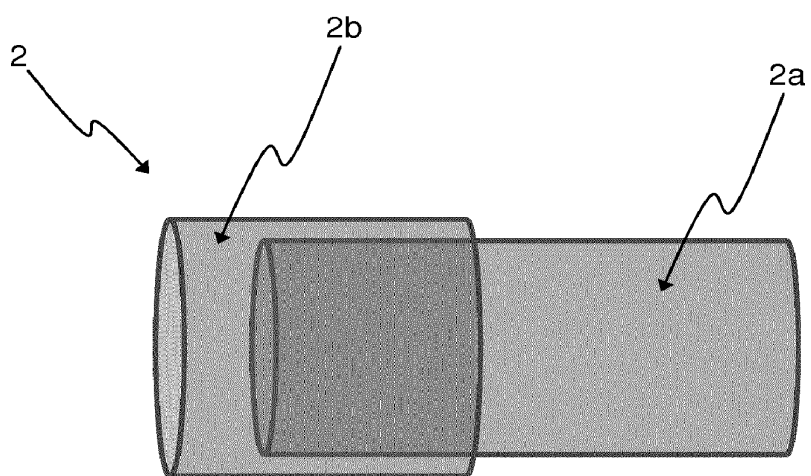


Figure 1

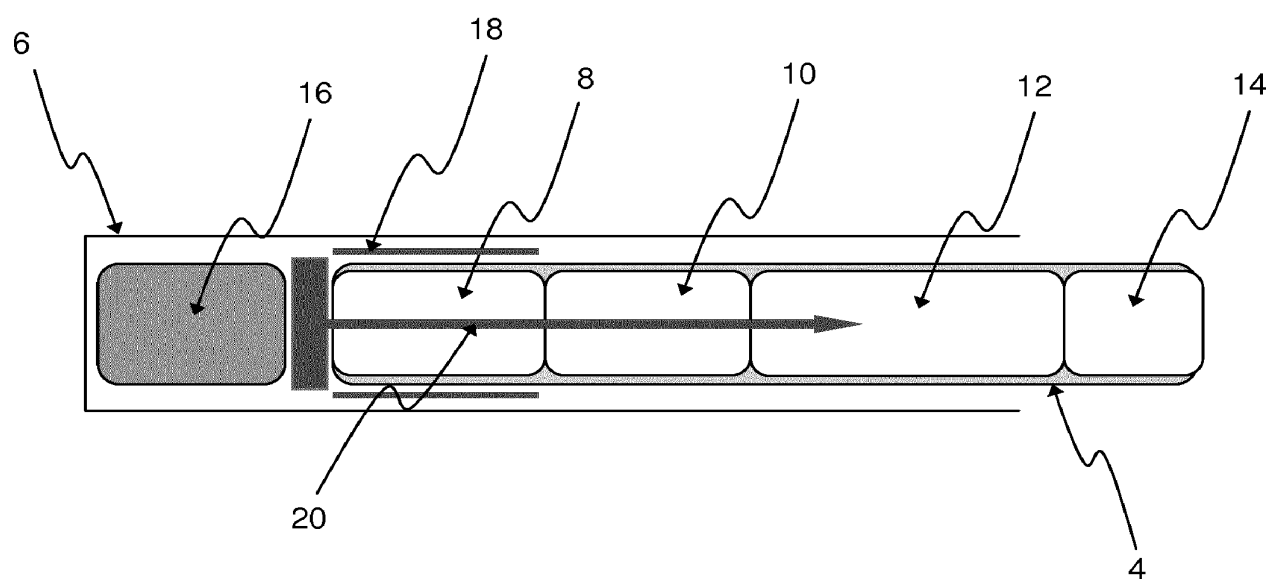


Figure 2

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/079496

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24F47/00

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F A61M A24B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/121610 A1 (UNIV DUKE [US]; ROSE JED E [US]; ROSE SETH D [US]; TURNER JAMES EDWARD) 9 October 2008 (2008-10-09) cited in the application	13-16
Y	paragraph [0233] - paragraph [0235]; figures 4-6	10-12
A	----- US 5 400 808 A (TURNER JAMES E [US] ET AL) 28 March 1995 (1995-03-28) column 1, line 65 - column 2, line 11	1-16
A	----- US 2010/006113 A1 (URTSEV VLADIMIR NIKOLAEVICH [RU] ET AL) 14 January 2010 (2010-01-14) paragraph [0044] ----- -/-	1-16



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

11 March 2015

Date of mailing of the international search report

18/03/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Leprêtre, François

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2014/079496

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2011/034723 A1 (UNIV DUKE [US]; ROSE JED E [US]; ROSE SETH D [US]; TURNER JAMES EDWARD) 24 March 2011 (2011-03-24) figures 4-6 -----	1-16
A	WO 2011/045609 A1 (BRITISH AMERICAN TOBACCO CO [GB]; WOODCOCK DOMINIC [GB]; MURPHY JAMES) 21 April 2011 (2011-04-21) page 3, line 5 - line 29 -----	1-16
X	US 4 858 630 A (BANERJEE CHANDRA K [US] ET AL) 22 August 1989 (1989-08-22)	1,2,6-9, 13,15,16
Y	column 7, line 30 - line 68 column 8, line 15 - line 25; examples -----	10-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/079496

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008121610	A1	09-10-2008	
		AU 2008232897 A1	09-10-2008
		CA 2682432 A1	09-10-2008
		CN 102014995 A	13-04-2011
		CN 103418062 A	04-12-2013
		EP 2134395 A1	23-12-2009
		EP 2708256 A2	19-03-2014
		JP 2010532672 A	14-10-2010
		JP 2013144157 A	25-07-2013
		US 2008241255 A1	02-10-2008
		WO 2008121610 A1	09-10-2008

US 5400808	A	28-03-1995	
		AT 174805 T	15-01-1999
		AU 642506 B2	21-10-1993
		BR 9106537 A	25-05-1993
		CA 2084771 A1	09-12-1991
		CN 1059649 A	25-03-1992
		DE 69130682 D1	04-02-1999
		DE 69130682 T2	20-05-1999
		DK 0591178 T3	23-08-1999
		EP 0591178 A1	13-04-1994
		ES 2127196 T3	16-04-1999
		FI 925552 A	07-12-1992
		GR 3029335 T3	28-05-1999
		HU 215018 B	28-08-1998
		IE 911956 A1	18-12-1991
		IL 98386 A	24-06-1994
		JP 3220139 B2	22-10-2001
		JP H05507639 A	04-11-1993
		LT 1493 A	26-06-1995
		LV 10692 A	20-06-1995
		NO 924714 A	08-02-1993
		NZ 238285 A	26-08-1994
		PT 97908 A	30-06-1993
		RU 2067876 C1	20-10-1996
		US 5167242 A	01-12-1992
		US 5400808 A	28-03-1995
		US 5501236 A	26-03-1996
		WO 9118636 A1	12-12-1991
		ZA 9104233 A	25-03-1992

US 2010006113	A1	14-01-2010	
		CA 2668047 A1	08-05-2008
		CN 101568269 A	28-10-2009
		EA 200701988 A1	30-06-2008
		EP 2084978 A1	05-08-2009
		IL 198382 A	31-07-2012
		JP 5131490 B2	30-01-2013
		JP 2010508034 A	18-03-2010
		NO 330556 B1	16-05-2011
		RU 2328192 C1	10-07-2008
		US 2010006113 A1	14-01-2010
		WO 2008052570 A1	08-05-2008

WO 2011034723	A1	24-03-2011	
		AU 2010295883 A1	12-04-2012
		CA 2774264 A1	24-03-2011
		CN 102612361 A	25-07-2012
		EP 2477607 A1	25-07-2012
		JP 2013505240 A	14-02-2013
		KR 20120104183 A	20-09-2012

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/079496

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		NZ 599060 A	31-10-2014
		RU 2012114814 A	27-10-2013
		US 2012255567 A1	11-10-2012
		WO 2011034723 A1	24-03-2011
-----		-----	-----
WO 2011045609 A1	21-04-2011	AR 080557 A1	18-04-2012
		AU 2010308117 A1	19-04-2012
		CA 2776247 A1	21-04-2011
		CN 102548431 A	04-07-2012
		EP 2488054 A1	22-08-2012
		ES 2439775 T3	24-01-2014
		JP 2013507906 A	07-03-2013
		KR 20120101654 A	14-09-2012
		RU 2012119709 A	27-11-2013
		US 2012298123 A1	29-11-2012
		US 2015013698 A1	15-01-2015
		WO 2011045609 A1	21-04-2011
-----		-----	-----
US 4858630 A	22-08-1989	AU 8196787 A	09-06-1988
		BG 49264 A3	16-09-1991
		BR 8706526 A	12-07-1988
		CA 1292163 C	19-11-1991
		CN 87108020 A	22-06-1988
		DD 264611 A5	08-02-1989
		DK 644687 A	09-06-1988
		EP 0270916 A2	15-06-1988
		FI 875391 A	09-06-1988
		IE 873000 L	08-06-1988
		JP S63148975 A	21-06-1988
		MA 21127 A1	01-07-1988
		NO 875085 A	09-06-1988
		PL 269339 A1	29-09-1988
		PT 86299 A	01-01-1988
		TR 23497 A	01-02-1990
		US 4858630 A	22-08-1989
		YU 218787 A	31-12-1988
		ZA 8708546 A	26-10-1988
-----		-----	-----

- | | |
|--|--|
| <p>(51) Classification internationale des brevets :
 G01N 27/18 (2006.01) A24F 47/00 (2006.01)</p> <p>(21) Numéro de la demande internationale :
 PCT/FR2015/050416</p> <p>(22) Date de dépôt international :
 20 février 2015 (20.02.2015)</p> <p>(25) Langue de dépôt : français</p> <p>(26) Langue de publication : français</p> <p>(30) Données relatives à la priorité :
 1451409 21 février 2014 (21.02.2014) FR</p> <p>(71) Déposant : SMOKIO [FR/FR]; 6 rue d'Alexandrie, F-75002 Paris (FR).</p> <p>(72) Inventeurs : LOUVEAU, Eric; 28bis, avenue Gaston Bourgeois, F-06600 Antibes (FR). MALCAVET, Didier; 9, passage du Lido, Résidence San Marco - C12, F-06800 Cagnes-sur-Mer (FR). ANAVI, Steve; 13 rue de Montmorency, F-75003 Paris (FR). PROT, Alexandre; 12, rue Dupetit-Thouars, F-75003 Paris (FR).</p> | <p>(74) Mandataires : DELUMEAU, François et al.; Cabinet Beau De Lomenie, 158 Rue de l'Université, 75340 Paris Cedex 07 (FR).</p> <p>(81) États désignés (<i>sauf indication contraire, pour tout titre de protection nationale disponible</i>) : AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.</p> <p>(84) États désignés (<i>sauf indication contraire, pour tout titre de protection régionale disponible</i>) : ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), eurasien (AM, AZ, BY, KG, KZ, RU, TJ, TM), européen (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).</p> |
|--|--|

[Suite sur la page suivante]

(54) Title : ELECTRONIC CIGARETTE

(54) Titre : CIGARETTE ELECTRONIQUE

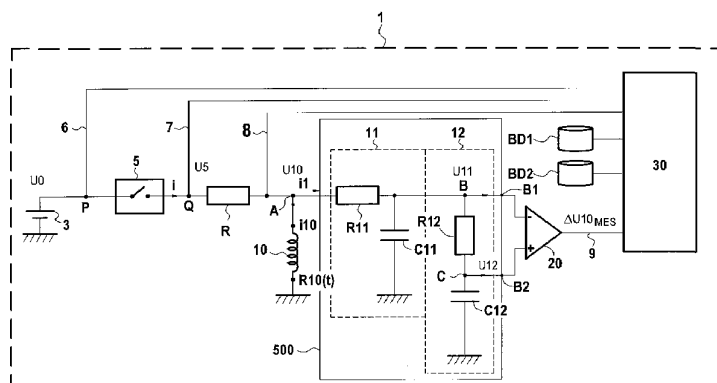


FIG. 1

(S7) Abstract : This electronic cigarette (1) comprises: - a heating element (10) able to vapourize a substrate during a smoking period; - means (30) for measuring an approximation (AUIOMESOO, UIOMESOO) of a characteristic of the voltage (U10(t)) across the terminals of the heating element (10) during this smoking period, said approximation being measured across the terminals (B1, B2) of a circuit (500) no component of which exhibits intrinsic characteristics not disturbed by the inhalations; - means (30) of estimating an approximation (AUIOTH(t), UIO-m(t)) of said characteristic of the voltage (U10(t)) across the terminals of the heating element (10) in the absence of inhalation during said smoking period; means (30) of calculating an intensity (F) representative of the intensity of the inhalations during said smoking period on the basis of an integration of the difference between said approximations during said smoking period; and - means (30) of estimating the said quantity of substrate vapourized by the heating element at least on the basis of said intensity.

(57) Abrégé :

[Suite sur la page suivante]



Publiée :

— avec rapport de recherche internationale (Art. 21(3))

Cette cigarette électronique (1) comporte : - un élément chauffant (10) apte à vaporiser un substrat pendant une période de fumage; - des moyens (30) de mesure d'une approximation ($\Delta U_{10_MES}(t)$, $U_{10_MES}(t)$) d'une caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant (10) pendant cette période de fumage, ladite approximation étant mesurée aux bornes (B1, B2) d'un circuit (500) dont aucun composant ne présente des caractéristiques intrinsèques ne sont pas perturbées par les inhalations; - des moyens (30) d'estimation d'une approximation ($\Delta U_{10_TH}(t)$, $U_{10_TH}(t)$) de ladite caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant (10) en l'absence d'inhalation pendant ladite période de fumage; - des moyens (30) de calcul d'une intensité (F) représentative de l'intensité des inhalations pendant ladite période de fumage à partir d'une intégration de la différence entre lesdites approximations pendant ladite période de fumage; et - des moyens (30) d'estimation de ladite quantité de substrat vaporisée par l'élément chauffant au moins à partir de ladite intensité.

Cigarette électronique

5 Arrière-plan de l'invention

L'invention se situe dans le domaine général des cigarettes électroniques comportant un élément chauffant apte à vaporiser un substrat en réponse aux inhalations de l'utilisateur, lorsque l'élément
10 chauffant est alimenté.

Plus précisément, l'invention propose une solution pour permettre d'estimer la quantité de substrat vaporisée par l'élément chauffant.

On connaît des solutions qui visent à estimer cette quantité en mesurant la variation de la résistivité de l'élément chauffant lorsque la
15 température de cet élément chauffant varie en raison des inhalations.

Le document EP 2 468 116 décrit en particulier une solution de ce type dans laquelle la résistivité d'un élément chauffant est calculée à partir de la différence de potentiels aux bornes de cet élément.

Malheureusement, la variation de la résistivité de l'élément
20 chauffant est très difficile à mesurer de sorte que ces solutions ne permettent pas d'estimer la quantité de substrat vaporisée de façon précise.

Objet et résumé de l'invention

25

Selon un premier aspect, l'invention concerne un procédé pour estimer la quantité de substrat vaporisée par un élément chauffant dans une cigarette électronique pendant une période de fumage.

Dans ce document, la notion de « vaporisation » est à prendre au
30 sens large ; elle désigne la transformation du substrat en gaz, y compris à une température inférieure à 100°C.

Ce procédé comporte :

- une étape de mesure d'une approximation d'une caractéristique de la tension aux bornes de l'élément chauffant pendant cette période de
35 fumage, cette approximation étant mesurée aux bornes d'un circuit dont

- aucun composant ne présente des caractéristiques intrinsèques perturbées par les inhalations ;
- une étape d'estimation d'une approximation de cette caractéristique de la tension aux bornes de l'élément chauffant en l'absence d'inhalation pendant la période de fumage ;
 - une étape de calcul d'une intensité représentative des inhalations pendant la période de fumage à partir d'une intégration de la différence entre lesdites approximations pendant ladite période de fumage ; et
 - une étape d'estimation de la quantité de substrat vaporisée par l'élément chauffant à partir de cette intensité et éventuellement d'autres paramètres.

Corrélativement, l'invention concerne une cigarette électronique comportant :

- un élément chauffant apte à vaporiser un substrat pendant une période de fumage, caractérisée en ce qu'elle comporte :
 - des moyens de mesure d'une approximation d'une caractéristique de la tension aux bornes de l'élément chauffant pendant cette période de fumage, cette approximation étant mesurée aux bornes d'un circuit dont aucun composant ne présente des caractéristiques intrinsèques perturbées par les inhalations ;
 - des moyens d'estimation d'une approximation de cette caractéristique de la tension aux bornes de l'élément chauffant en l'absence d'inhalation pendant la période de fumage ;
 - des moyens de calcul d'une intensité des inhalations pendant la période de fumage à partir d'une intégration de la différence entre lesdites approximations pendant ladite période de fumage ; et
 - des moyens d'estimation de ladite quantité de substrat vaporisée par l'élément chauffant à partir de cette intensité et éventuellement d'autres paramètres.

- Ainsi, et d'une façon générale, l'invention propose d'estimer la quantité de substrat vaporisé pendant une période de fumage, en comparant les caractéristiques de la tension aux bornes de l'élément chauffant, avec ces caractéristiques en l'absence d'inhalation. Mais de façon très avantageuse, l'invention ne mesure pas directement ces caractéristiques mais des estimations aux bornes d'un circuit dont les caractéristiques intrinsèques ne sont pas perturbées par les inhalations.

Grâce à cette caractéristique particulièrement avantageuse, l'invention permet d'estimer de façon très fiable l'intensité de ces inhalations, et donc d'améliorer considérablement l'estimation de la quantité de substrat vaporisée.

5 De façon très avantageuse, le circuit précité, aux bornes duquel on réalise les mesures pour estimer les caractéristiques de la tension aux bornes de l'élément chauffant, ne comporte lui-même aucun élément chauffant. Cette caractéristique permet avantageusement de limiter la puissance consommée pour la détection de la quantité de substrat
10 vaporisée, de sorte qu'une très large majorité de la puissance totale consommée par la cigarette électronique est utilisée pour vaporiser le substrat. Le dispositif de l'invention pour mesurer la quantité de substrat vaporisée par une cigarette électronique ne présente donc pas les inconvénients du dispositif décrit dans le document EP 2 143 346.

15 Dans un mode de réalisation de l'invention, la quantité déterminée de substrat vaporisée est utilisée pour estimer la quantité ou la qualité de composants inhalés par l'utilisateur, par exemple une quantité de nicotine.

Dans une première variante de réalisation de l'invention, on estime la variation de la tension aux bornes de l'élément chauffant.

20 Dans un premier mode de réalisation de cette première variante, on calcule une approximation de la variation de la tension aux bornes de l'élément chauffant à partir de tensions mesurées aux bornes d'au moins deux éléments, les tensions aux bornes de chacun de ces éléments donnant une approximation de la tension aux bornes de l'élément
25 chauffant à des instants légèrement décalés dans le temps.

Dans ce mode de réalisation de l'invention, la cigarette électronique selon l'invention comporte :

- au moins deux éléments, la tension aux bornes de chacun desdits éléments donnant une approximation de la tension aux bornes dudit
30 élément chauffant à des instants légèrement décalés dans le temps, et
- des moyens pour mesurer une approximation de la variation de la tension aux bornes de l'élément chauffant à partir des tensions mesurées aux bornes desdits éléments.

35 L'invention permet de suivre l'évolution dans le temps des caractéristiques de la tension aux bornes de l'élément chauffant, non pas à l'aide d'un outil qui suivrait précisément et directement en temps réel

cette tension, mais en créant un retard artificiel delta entre deux éléments de la cigarette électronique, ce retard permettant d'obtenir à un instant t une estimation de l'évolution de la tension aux bornes des moyens de chauffage entre l'instant t -delta et l'instant t .

5 Dans un mode de réalisation, ces éléments sont des circuits RC série connectés en série.

Dans un deuxième mode de réalisation de cette première variante, l'approximation de la variation de la tension aux bornes de l'élément chauffant est la dérivée par rapport au temps d'une différence de
10 potentiels mesurée aux bornes d'une résistance de mesure connectée en série avec l'élément chauffant.

Dans une deuxième variante de réalisation de l'invention, on estime la tension aux bornes de l'élément chauffant.

Dans un mode de réalisation de cette deuxième variante,
15 l'approximation de la tension aux bornes de l'élément chauffant est la tension mesurée aux bornes d'une résistance de mesure connectée en série avec ledit élément chauffant.

Dans ce mode de réalisation, la cigarette électronique comporte des moyens aptes à mesurer une différence de potentiel aux bornes d'une
20 résistance de mesure connectée en série avec l'élément chauffant, et des moyens pour mesurer une approximation de la variation de la tension aux bornes de l'élément chauffant à partir de ladite différence de potentiels.

Brève description des dessins

25 D'autres caractéristiques et avantages de la présente invention ressortiront de la description faite ci-dessous, en référence aux dessins annexés qui en illustrent un exemple de réalisation dépourvu de tout caractère limitatif. Sur ces figures :

- 30 - la figure 1 représente un premier mode de réalisation d'une cigarette électronique conforme à l'invention ;
- la figure 2 représente la variation de tension aux bornes de différents composants de la cigarette électronique de la figure 1 suite à une inhalation ;
- la figure 3 représente la différence théorique entre les tensions de
35 sortie de deux circuits RC de la figure 1, en l'absence d'inhalation ;

- la figure 4 illustre une méthode pour calculer une intensité d'inhalation dans la cigarette électronique de la figure 1
- la figure 5 représente des détails d'une cigarette électronique conforme à un deuxième mode de réalisation de l'invention;
- 5 - la figure 6 représente des détails d'une cigarette électronique conforme à un troisième mode de réalisation de l'invention;
- la figure 7 illustre une méthode pour calculer une intensité d'inhalation dans la cigarette électronique de la figure 6 ; et
- la figure 8 représente des détails d'une cigarette électronique
- 10 - la figure 9 représente, sous forme d'organigramme, les principales étapes d'un procédé d'estimation conforme à un mode particulier de réalisation de l'invention.

15

Description détaillée d'un premier mode de réalisation de l'invention

Nous allons maintenant décrire en référence à la figure 1 un premier mode de réalisation d'une cigarette électronique 1 conforme à

20 l'invention, figure dans laquelle seuls les composants électroniques utiles à la compréhension de ce mode de réalisation ont été représentés.

La cigarette électronique 1 comporte un élément chauffant 10 apte à vaporiser un substrat, la résistivité $R_{10}(t)$ de cet élément chauffant étant susceptible de varier en fonction de sa température.

25 Dans ce mode de réalisation, l'élément chauffant 10 comporte une première borne non référencée reliée à la masse et une deuxième borne A, de sorte que le potentiel U_{10} de cette borne correspond à la tension aux bornes de l'élément chauffant 10.

Conformément à l'invention, la cigarette électronique 1 comporte

30 une batterie 3 apte à délivrer une tension U_0 , et un interrupteur 5 connecté à une borne P de la batterie, pour alimenter, uniquement lorsque l'utilisateur appuie sur un bouton non représenté, l'élément chauffant 10 à partir de la batterie 3.

Dans le mode de réalisation décrit ici, la tension U_0 présente une

35 tension nominale de l'ordre de 3.7V et une courbe de décharge dans une plage [4.2V, 0V].

Lorsque l'interrupteur 5 est en position fermée, un courant électrique d'intensité i traverse cet interrupteur et un courant électrique d'intensité i_{10} traverse l'élément chauffant 10.

De manière à pouvoir mesurer les variations de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10, la cigarette électronique 1 comporte, dans ce mode de réalisation, une résistance de mesure R placée en série entre une borne Q de l'interrupteur 5 et la borne A de l'élément chauffant 10. La résistance de mesure est traversée par le courant électrique d'intensité i lorsque l'interrupteur 5 est en position fermée. Les caractéristiques intrinsèques de la résistance de mesure R ne sont pas perturbées par les inhalations.

Du fait de cet agencement particulier, et en considérant que l'interrupteur 5 est un interrupteur parfait (c'est-à-dire sans perte, donc avec $U_5 = U_0$), on obtient, de façon connue :

$$U_{10}(t) = U_0.R_{10}(t)/(R+R_{10}(t)) \quad (1)$$

Par conséquent, les variations de la résistivité $R_{10}(t)$ de l'élément chauffant 10 s'accompagnent d'une variation de la tension $U_{10}(t)$ aux bornes de l'élément chauffant.

La figure 2 représente en ordonnée la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 en fonction du temps, figure sur laquelle quatre événements se produisant à des instants t_1 à t_4 ont été représentés :

- t_1 : appui sur le bouton fermant l'interrupteur 5. La tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 qui était nulle, atteint presque instantanément une tension très proche de la tension U_0 de la batterie 3. A partir, de cet instant t_1 et tant que l'utilisateur n'inhale pas, la température de l'élément chauffant 10 augmente jusqu'à atteindre une température limite, sa résistivité $R_{10}(t)$ augmente et la tension $U_{10}(t)$ augmente.
- t_2 et t_3 : début et arrêt de l'inhalation. L'inhalation amène un flux d'air froid sur l'élément chauffant 10 avec pour effet de baisser sa température, diminuer sa résistivité $R_{10}(t)$ et donc de baisser la tension $U_{10}(t)$ à ses bornes. Inversement, la fin de l'inhalation entraîne, si l'interrupteur 5 est maintenu fermé, un réchauffement de l'élément chauffant, et une augmentation de la tension à ses bornes.

- t4 : relâche du bouton et ouverture de l'interrupteur 5 : l'élément chauffant 10 n'est plus alimenté par la batterie 3 et la tension $U_{10}(t)$ à ses bornes redevient nulle presque instantanément.

5 Dans ce document, on appelle « période de fumage », la période de temps entre les instants t1 et t4, à savoir la période au cours de laquelle l'utilisateur appuie sur le bouton commandant l'interrupteur 5 en position fermée. Pendant cette période, l'utilisateur peut éventuellement ne pas inhaler ou inhaler une ou plusieurs bouffées.

10 Dans ce premier mode particulier de réalisation de l'invention, on estime la quantité de substrat vaporisée pendant une période de fumage en comparant une mesure $\Delta U_{10_MES}(t)$ d'une approximation de la variation de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 pendant cette période de fumage avec une estimation théorique $\Delta U_{10_TH}(t)$ de cette approximation de cette variation de tension en l'absence de toute
15 inhalation pendant la période de fumage.

Plus précisément, dans ce mode de réalisation de l'invention, on choisit, comme approximation de la variation de tension à l'instant t aux bornes de l'élément chauffant 10, la différence entre deux tensions $U_{11}(t)$ et $U_{12}(t)$ mesurées aux bornes B1, B2 d'un circuit 500 comprenant deux
20 sous-circuits 11,12 distincts et de même type, les tensions $U_{11}(t)$ et $U_{12}(t)$ aux bornes de ce circuit 500 étant des approximations de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 à deux instants légèrement décalés dans le temps.

Il est fondamental de constater qu'aucun des composants du circuit
25 500 n'a de caractéristique intrinsèque perturbée par les inhalations.

Dans le mode de réalisation décrit ici, on utilise deux sous-circuits RC série 11,12, placés en série entre l'élément chauffant 10 et des moyens 30 de calcul aptes à calculer la différence entre les tensions $U_{11}(t)$ et $U_{12}(t)$.

30 Dans le mode de réalisation décrit ici, les tensions $U_{11}(t)$ et $U_{12}(t)$ sont les potentiels des points B et C représentés à la figure 1.

La constante de temps T12 du deuxième circuit RC 12 est choisie largement supérieure à celle T11 du premier circuit RC 11, par exemple d'un facteur 100.

35 Dans le mode de réalisation décrit ici, on utilise un amplificateur 20 de gain G pour amplifier la différence $\Delta U_{10}(t)$ entre $U_{11}(t)$ et $U_{12}(t)$.

Dans le mode de réalisation décrit ici, les résistances R11 et R12 des sous-circuits RC 11 et 12 sont négligeables par rapport à l'impédance de l'amplificateur 20.

Par conséquent,

$$\Delta U_{10}(t) = G.(U_{12}(t) - U_{11}(t))$$

Dans le mode de réalisation décrit ici :

- le gain G est choisi dans la plage [100 ; 10000], par exemple égal à 500 ;
- la différence $U_{12}(t) - U_{11}(t)$ est de l'ordre de quelques dizaines de microvolts ; et
- $\Delta U_{10}(t)$ est de l'ordre de quelques dizaines voire centaines de microvolts et mesurable par les moyens de calcul 30.

Sur la figure 2, on a également représenté les tensions de sortie $U_{11}(t)$ et $U_{12}(t)$ des sous-circuits RC série 11 et 12.

- 15 Comme expliqué précédemment, lorsque l'utilisateur appuie sur le bouton à l'instant t_1 , l'élément chauffant 10 est alimenté et la tension $U_{10}(t)$ à ses bornes augmente. Les deux capacités C11, C12 des sous-circuits RC 11, 12 se chargent, la deuxième et plus importante capacité C12 étant en retard par rapport à la première et plus petite capacité C11.
- 20 On observe par conséquent, entre l'appui sur le bouton (t_1) et le début de l'inhalation (t_2) que $U_{12}(t) < U_{11}(t) < U_{10}(t)$.

- Lorsque l'utilisateur commence à inhaler à l'instant t_2 , l'élément chauffant 10 se refroidit et la tension $U_{10}(t)$ à ses bornes diminue. La deuxième et plus importante capacité C12, est en retard par rapport à la première et plus petite capacité C11. On observe pendant toute la durée de l'inhalation, à savoir entre t_2 et t_3 que $U_{12}(t) > U_{11}(t) > U_{10}(t)$.
- 25

Lorsque l'utilisateur arrête d'inhaler à l'instant t_3 , l'élément chauffant 10 se réchauffe et la tension $U_{10}(t)$ à ses bornes augmente. On retrouve alors la situation dans laquelle $U_{12}(t) < U_{11}(t) < U_{10}(t)$.

- 30 Peu de temps après que l'utilisateur relâche le bouton à l'instant t_4 , la tension $U_{10}(t)$ redevient nulle, les capacités C11 et C12 se déchargent et leurs tensions de sortie $U_{11}(t)$, $U_{12}(t)$ redeviennent nulles.

- De façon connue, on distingue, lorsqu'on applique une tension constante aux bornes d'une capacité, un régime transitoire au cours duquel la capacité se charge progressivement jusqu'à atteindre une charge limite fonction de sa valeur et un régime permanent durant lequel
- 35

la charge de la capacité reste à cette valeur limite tant que l'on continue à lui appliquer cette tension constante.

La figure 2 correspond à la situation dans laquelle l'utilisateur commence à inhaler (instant t_2) en régime permanent. L'homme du métier comprendra que si l'utilisateur commençait à inhaler pendant le régime transitoire, la grande capacité C_{12} n'étant pas entièrement chargée, la tension de sortie $U_{12}(t)$ de la deuxième capacité ne deviendrait pas nécessairement supérieure à la tension de sortie $U_{11}(t)$ de la première capacité.

Dans le mode de réalisation décrit ici, le système formé par les deux sous-circuits 11 et 12 est en régime transitoire pendant environ 800 ms après l'instant t_1 auquel l'utilisateur appuie sur le bouton.

La figure 3, qui représente la différence $\Delta U_{10TH}(t)$ théorique entre les tensions de sortie $U_{11}(t)$ et $U_{12}(t)$ des deux sous-circuits RC 11, 12 en l'absence d'inhalation, autrement dit une approximation théorique de la variation de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 à l'instant t , illustre ces différents régimes.

Pendant le régime transitoire, $U_{12}(t)$ est toujours inférieure à $U_{11}(t)$ mais comme représenté à la figure 2 la valeur absolue de la différence entre ces deux tensions augmente puis diminue jusqu'à atteindre une valeur constante α en régime permanent.

Dans le mode de réalisation décrit ici, cette constante α peut être négligée et supposée nulle par la suite.

En régime transitoire, et en notant :

- R_{11} , la résistance du premier sous-circuit RC série 11 ;
- C_{11} , la capacité du premier sous-circuit RC série 11 ;
- R_{12} , la résistance du deuxième sous-circuit RC série 12 ;
- C_{12} , la capacité du deuxième sous-circuit RC série 12 ;
- T_{11} la constante de temps $R_1.C_1$ du premier sous-circuit RC série 11 ; et
- T_{12} la constante de temps $R_2.C_2$ du deuxième sous-circuit RC série 12 ;

on obtient, de façon théorique :

$$U_{11TH}(t) = U_{10}(t).(1 - \exp(-t/T_{11}))$$

$$U_{12TH}(t) = U_{11TH}(t).(1 - \exp(-t/T_{12}))$$

$$\text{soit } U_{12TH}(t) = U_{10}(t).(1 - \exp(-t/T_{11})).(1 - \exp(-t/T_{12}))$$

Par conséquent, la variation théorique $\Delta U_{10_{TH}}(t)$ de la tension aux bornes de l'élément chauffant 10 s'exprime :

$$\Delta U_{10_{TH}}(t) = G.(U_{11_{TH}}(t) - U_{12_{TH}}(t))$$

5 soit $\Delta U_{10_{TH}}(t) = G.U_{10}(t).(1 - \exp(-t/T_{11})).(\exp(-t/T_{12}))$

ou encore avec (1)

$$\Delta U_{10_{TH}}(t) = G.[U_0.R_{10}(t)/(R+R_{10}(t))].(1 - \exp(-t/T_{11})).(\exp(-t/T_{12}))$$

10 En faisant l'approximation que $R_{10}(t)$ est constant pendant la période de fumage et égal à $R_{10}(t_1)$, on obtient finalement l'expression de $\Delta U_{10_{TH}}(t)$:

- en régime transitoire :

$$\Delta U_{10_{TH}}(t) = G.[U_0.R_{10}(t_1)/(R+R_{10}(t_1))].(1 - \exp(-t/T_{11})).(\exp(-t/T_{12})) \quad (2)$$

15 - en régime permanent :

$$\Delta U_{10_{TH}}(t) = \alpha = 0.$$

20 Dans le mode de réalisation de la figure 1, l'approximation $\Delta U_{10_{MES}}(t)$ de la variation de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 est la tension de sortie des moyens d'amplification 20, à savoir le potentiel de la borne 9.

25 Dans le mode de réalisation décrit ici, la quantité de substrat vaporisée pendant une période de fumage est estimée à partir d'une intensité d'inhalation F calculée par intégration de la différence au cours d'une période de fumage, entre l'approximation $\Delta U_{10_{MES}}(t)$ de la variation de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 pendant cette période de fumage et l'estimation théorique $\Delta U_{10_{TH}}(t)$ de cette approximation de cette variation de tension en l'absence de toute inhalation pendant la période de fumage.

30 Cette intensité d'inhalation F correspond, dans l'exemple de réalisation décrit ici, à l'aire hachurée Figure 4. Cette aire peut notamment être calculée par une somme de Riemann avec un pas de 20ms entre les instants t_2 et t_4 .

35 Dans l'exemple de réalisation décrit ici, t_2 est déterminé comme étant l'instant où la valeur absolue de la différence $\Delta U_{10_{MES}}(t)$ et $\Delta U_{10_{TH}}(t)$ devient supérieure à un seuil S_{T2} prédéterminé:

$$|\Delta U_{10_{MES}}(t_2) - \Delta U_{10_{TH}}(t_2)| > S_{T2}$$

L'instant t_4 est l'instant où l'utilisateur relâche le bouton.

Pour calculer l'intensité d'inhalation F par la méthode de Riemann, on évalue et on mémorise $\Delta U_{10_{MES}}(t)$ et $\Delta U_{10_{TH}}(t)$, à différents instants entre t1 et t4, par exemple toutes les 20ms. Dans ce mode de réalisation :

1. $\Delta U_{10_{MES}}(t)$ est la mesure du potentiel de la borne 9 à l'instant t
2. $\Delta U_{10_{TH}}(t)$ entre t_1 et $t_1+800ms$ (régime transitoire) est lue dans un enregistrement d'une première base de données BD1 construite lors de tests préliminaires effectuées en laboratoire et mémorisée dans la cigarette électronique 1, l'enregistrement étant sélectionné en fonction des paramètres de l'équation (2).
3. $\Delta U_{10_{TH}}(t) = 0$, entre $t_1+800ms$ et t_4 (régime permanent)

De retour à l'équation (2), l'expression de $\Delta U_{10TH}(t)$ en régime transitoire dépend de six paramètres, à savoir :

- 15
- le gain G de l'amplificateur 20 ;
 - la tension U_0 délivrée par la batterie 3 ;
 - la résistivité $R_{10}(t_1)$ de l'élément chauffant supposée constante ;
 - la valeur de la résistance de mesure R ;
 - les constantes de temps T_{11} et T_{12} des sous-circuits RC 11 et 12.

20 Dans le mode de réalisation décrit ici, et de retour à la figure 1, les moyens de calcul 30 sont aptes à mesurer la tension U_0 à la borne P de la batterie 3 au moyen d'une sonde de tension 6.

Dans le mode de réalisation décrit ici, les moyens de calcul 30 sont également aptes à estimer la résistivité $R_{10}(t_1)$ de l'élément chauffant.

25 Pour cela, les moyens de calcul 30 mesurent, à l'instant t1, les tensions U5 à la borne Q de l'interrupteur 5 au moyen d'une sonde de tension 7 et la tension U10 à la borne A de l'élément chauffant 10 au moyen d'une sonde de tension 8.

En notant i l'intensité du courant électronique qui traverse la
30 résistance R , on obtient par application de la loi des nœuds à la borne A,
et de la loi d'Ohm à la résistance R , on obtient $i_1 + i_{10} = (U_5 - U_{10})/R$.

Or, dans le mode de réalisation décrit ici, i_1 est négligeable devant i_{10} . Par conséquent, par application de la loi d'Ohm à l'élément chauffant 10 :

$$35 \quad R_{10} = R \cdot U_{10} / (U_5 - U_{10}) \quad (3)$$

Dans le mode de réalisation de l'invention décrit ici, la première base de données BD1 mémorise, pour une pluralité de six-uplet correspondant aux 6 paramètres {G, U0, R10, R, T11, T12}, des valeurs de la tension théorique $\Delta U_{10-TH}(t)$ en l'absence d'inhalation et en régime transitoire à différents instants t comptés entre t1 et t1+800ms.

Les moyens de calcul sont donc en mesure de calculer l'intensité d'inhalation F par la méthode de Riemann.

Dans le mode de réalisation décrit ici, les moyens de calcul 30 interrogent une deuxième base de données BD2 de la cigarette électronique 1 pour déterminer la quantité de substrat vaporisée pendant la période de fumage en fonction de quatre paramètres :

- durée t4 – t1 de la période de fumage ;
- tension U0 de la batterie 3 mesurée par les moyens de calcul 30 ;
- résistance R10(t1) de l'élément chauffant 10, supposée constante au cours d'une période de fumage, et mesurée par les moyens de calcul 30 ; et
- intensité d'inhalation F, calculée ici par la méthode de Riemann.

En variante d'autres paramètres peuvent aussi être utilisés et notamment la température de l'élément chauffant 10 à t1, la viscosité du substrat, la vitesse d'évaporation du substrat, la fonction de transfert de l'élément chauffant 10 caractérisant son refroidissement, la densité de gouttes de substrat vaporisée en fonction de l'intensité d'inhalation F, ...

Dans le mode de réalisation décrit ici, la tension U0 de la batterie 3 est mesurée par les moyens de calcul 30. En variante, cette tension pourrait être considérée constante et égale à la valeur nominale de la batterie.

Description d'un deuxième mode de réalisation de l'invention

Dans le mode de réalisation de la figure 1, on utilise 2 sous-circuits RC série 11, 12 en série et un amplificateur 20 pour estimer la variation de tension $\Delta U_{10}(t)$ aux bornes de l'élément chauffant 10.

En variante, et comme représenté à la figure 5, on peut par exemple utiliser un circuit 500 comportant trois sous-circuits RC et deux amplificateurs 20₁, 20₂.

Dans ce mode de réalisation :

- le premier sous-circuit RC (R11/C11) suit de très près la tension aux bornes de l'élément chauffant R10 et représente une estimation de la tension aux bornes de l'élément chauffant R10(t) à l'instant t de la mesure ;
- 5 - le deuxième sous-circuit RC (R12/C12) suit avec un léger retard dt la tension aux bornes de l'élément chauffant R10 et représente une estimation de ce qu'était la tension R10(t-dt) aux bornes de l'élément chauffant R10 à un instant passé t-dt proche de l'instant t de la mesure ;
- le troisième sous-circuit RC (R13/C13) suit avec un retard plus important
- 10 Dt la tension aux bornes de l'élément chauffant R10 et représente une estimation de ce qu'était la tension R10(t-Dt) aux bornes de l'élément chauffant R10 à un instant passé t-Dt plus éloigné de l'instant t de la mesure.

A cet effet, les constantes de temps des trois sous-circuits RC sont

15 choisies de sorte que l'équation ci-dessous soit vérifiée :

$$R11.C11 < R12.C12 < R13.C13 ;$$

De plus, pour un suivi plus fin, il peut être plus optimal d'avoir en plus l'équation suivante vérifiée :

$$(R11.C11) / (R12.C12) < (R12.C12) / (R13.C13)$$

20 Aucun des composants du circuit 500 n'a de caractéristique intrinsèque perturbée par les inhalations.

Dans ce mode de réalisation, le circuit 500 présente quatre bornes B1, B2, B3 et B4.

25 Comme dans le premier mode de réalisation, la quantité de substrat vaporisée pendant une période de fumage est estimée à partir d'une intensité d'inhalation F calculée par intégration de la différence au cours d'une période de fumage, entre l'approximation de la variation de la tension U10(t) aux bornes de l'élément chauffant 10 pendant cette période de fumage et l'estimation théorique $\Delta U10_{TH}(t)$ de cette

30 approximation de cette variation de tension en l'absence de toute inhalation pendant la période de fumage.

Mais de façon très avantageuse, on réalise dans ce mode de réalisation, deux approximations $\Delta U10^1_{MES}(t)$ et $\Delta U10^2_{MES}(t)$ de la variation de la tension U10(t) aux bornes de l'élément chauffant 10 pendant la

35 période de fumage, la première approximation étant mesurée aux bornes

B1 et B2 du circuit 500, la deuxième approximation étant mesurée aux bornes B3 et B4 du circuit 500.

Ce mode de réalisation permet d'améliorer l'estimation des variations de tension aux bornes de l'élément chauffant 10, et ce quelles que soient les caractéristiques de la bouffée.

En effet, grâce au choix des constantes de temps :

- la tension mesurée aux bornes B1 et B2 du circuit 500 est particulièrement représentative de la tension aux bornes de l'élément chauffant R10 pour un certain type d'inhalation, par exemple une inhalation rapide et/ou intense ou saccadée; alors que
- la tension mesurée aux bornes B3 et B4 du circuit 500 est particulièrement représentative de la tension aux bornes de l'élément chauffant R10 pour un autre type d'inhalation, par exemple une inhalation lente et/ou légère ou continue.

On construit alors dans ce mode de réalisation les 2 courbes $\Delta U_{10\text{MES}}(t)$ et $\Delta U_{10\text{TH}}(t)$ suivantes :

$$\begin{aligned} - \Delta U_{10\text{MES}}(t) &= K1 \Delta U_{10\text{MES}}^1(t) + K2 \Delta U_{10\text{MES}}^2(t) \\ - \Delta U_{10\text{TH}}(t) &= K1 \Delta U_{10\text{TH}}^1(t) + K2 \Delta U_{10\text{TH}}^2(t) \end{aligned}$$

dans lesquelles $\Delta U_{10\text{TH}}^1(t)$ et $\Delta U_{10\text{TH}}^2(t)$ sont des estimations théoriques des approximations $\Delta U_{10\text{MES}}^1(t)$ et $\Delta U_{10\text{MES}}^2(t)$ en l'absence de toute inhalation pendant la période de fumage.

On retient alors, pour calculer l'intensité F de l'inhalation, l'aire entre ces deux courbes $\Delta U_{10\text{MES}}$ et $\Delta U_{10\text{TH}}$.

Les coefficients K1 et K2 sont fixes et déterminés en fonction des constantes de temps des circuits RC (les valeurs R11.C11, R12.C12 et R13.C13).

De façon non limitative, ce couple de coefficients pourrait être choisi conformément à l'un des quatre exemples suivants :

Exemple 1 :

$$\begin{aligned} K1 &= 1/2 ; \\ K2 &= 1/2 \end{aligned}$$

Exemple 2 :

$$K1 = (R11.C11+R12.C12)/(R11.C11+2.R12.C12+R13.C13) ;$$

$$K2 = (R12.C12+R13.C13)/(R11.C11+2.R12.C12+R13.C13)$$

5

Exemple 3 :

$$K1 = R12.C12/(R11.C11) / ((R12.C12)/(R11.C11) + (R13.C13)/(R12.C12))$$

$$K2 = R13.C13/(R12.C12) / ((R12.C12)/(R11.C11) + (R13.C13)/(R12.C12))$$

10 Exemple 4 :

$$K1 = (R12.C12-R11.C11) / (R13.C13-R11.C11) ;$$

$$K2 = (R13.C13-R12.C12) / (R13.C13-R11.C11)$$

15 Pour s'assurer une bonne exploitation, ces coefficients peuvent testés/validés en laboratoire.

Description d'un troisième mode de réalisation de l'invention

20 Dans le mode de réalisation de la figure 6, la grandeur de la tension aux bornes de l'élément chauffant que l'on estime n'est pas la variation $\Delta U_{10}(t)$ de cette tension mais la valeur $U_{10}(t)$ de cette tension elle-même.

Dans ce mode de réalisation de l'invention, on estime cette valeur $U_{10}(t)$ en mesurant la tension $U_5 - U_{10}$ aux bornes B1 et B2 d'un circuit 500 constitué dans cet exemple par la résistance de mesure R.

25 En effet, en reprenant l'équation (3) :

$$U_{10}(t) = R_{10} / R . (U_5 - U_{10}) (t) \quad (4)$$

30 Ce mode de réalisation nécessite de connecter des moyens de calcul aux bornes B1 et B2 de la résistance de mesure R pour mesurer précisément les variations de $U_5 - U_{10}$.

La figure 7 représente :

- l'approximation $U_{10_MES}(t)$ de la tension $U_{10}(t)$ aux bornes de l'élément chauffant 10 pendant la période de fumage, calculée en utilisant l'équation

(4), la différence de $(U5 - U10)(t)$ étant la différence de potentiels mesurés par les moyens de calcul 30 de la figure 6 entre les points B1 et B2 ;

- l'estimation de l'approximation $U10_{TH}(t)$ aux bornes de l'élément chauffant 10 en l'absence d'inhalation pendant ladite période de fumage,
- l'intensité F de l'inhalation correspondant à l'intégration de la différence entre $U10_{MES}(t)$ et $U10_{TH}(t)$ pendant la période de fumage.

Description d'un quatrième mode de réalisation de l'invention

Dans un quatrième mode de réalisation représenté à la figure 8, pour estimer la variation $\Delta U_{MES10}(t)$ de la tension aux bornes de l'élément chauffant 10, on effectue, comme pour le premier mode de réalisation, la différence entre deux tensions $U12(t)$ et $U11(t)$ aux bornes B1 et B2 d'un circuit 500, chacune de ces tensions donnant une approximation de la tension aux bornes de l'élément chauffant (10) à des instants légèrement décalés dans le temps.

Dans ce mode de réalisation, on utilise, pour générer ce retard, un circuit 500 constitué par une ligne de retard 90 entre les points de mesure des tensions $U11(t)$ et $U12(t)$.

Cette ligne de retard peut par exemple être constituée par :

- une grande capacité ;
- un convertisseur analogique numérique couplé à un convertisseur numérique analogique.

Les caractéristiques intrinsèques de la ligne de retard 90 ne sont pas perturbées par les inhalations.

Description d'un cinquième mode de réalisation de l'invention

Dans un quatrième mode de réalisation de l'invention, on peut aussi estimer la variation $\Delta U_{MES10}(t)$ de la tension aux bornes de l'élément chauffant 10, en calculant la dérivée par rapport au temps de la tension mesurée $U10_{MES}(t)$, comme dans le troisième mode de réalisation, avec le moyens de calcul 30 de la figure 6 entre les points B1 et B2.

Cette valeur peut être comparée avec la variation théorique $\Delta U_{TH10}(t)$ de la tension aux bornes de l'élément chauffant 10 en l'absence d'inhalation, comme dans le premier mode de réalisation.

La figure 9 représente sous forme d'organigramme un procédé d'estimation de la quantité de substrat vaporisée conforme à un mode particulier de réalisation de l'invention.

5 Ce procédé peut par exemple être mis en œuvre par les moyens de calcul 30 de la cigarette électronique de la figure 1.

Au cours d'une étape E10, les moyens de calcul 30 détectent l'appui sur le bouton entraînant la fermeture de l'interrupteur 5. L'instant t_1 de cette détection est enregistré en mémoire.

10 Au cours d'une étape E20, juste après cette détection, les moyens de calcul 30 mesurent la tension U_0 délivrée par la batterie 3 et la résistivité $R_{10}(t_1)$ de l'élément chauffant.

Toutes les 20ms, au cours d'une étape E30, jusqu'à l'instant t_4 de détection de la relâche du bouton entraînant l'ouverture de l'interrupteur
15 5, les moyens de calcul 30 :

- mesurent $\Delta U_{10_MES}(t)$ (potentiel de la borne 9) ;
- estiment $\Delta U_{10_TH}(t)$ par lecture de la première base de données BD1 entre t_1 et $t_1+800ms$. Entre $t_1+800ms$ et t_4 , ils estiment $\Delta U_{10_TH}(t) = 0$.

20 Au cours d'une étape E40, les moyens de calcul 30 estiment l'instant t_2 du début de la bouffée, cet instant étant le premier instant après t_1 tel que $|\Delta U_{10_MES}(t_2) - \Delta U_{10_TH}(t_2)| > S_{T2}$.

Au cours d'une étape E50, les moyens de calcul 30 calculent l'intensité F de l'inhalation comme l'intégration de la différence entre
25 $\Delta U_{10_MES}(t)$ et $\Delta U_{10_TH}(t)$ entre t_2 et t_4 .

Au cours d'une étape E60, les moyens de calcul 30 estiment la quantité de substrat vaporisé entre t_2 et t_4 en interrogeant la deuxième base de données B2.

REVENDEICATIONS

- 5 1. Procédé d'estimation de la quantité de substrat vaporisée par un élément chauffant (10) dans une cigarette électronique (1) pendant une période de fumage, caractérisé en ce qu'il comporte :
- une étape (E30) de mesure d'une approximation ($\Delta U_{10_{MES}}(t)$, $U_{10_{MES}}(t)$) d'une caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément
 - 10 chauffant (10) pendant cette période de fumage, ladite approximation étant mesurée aux bornes (B1, B2) d'un circuit (500) dont aucun composant ne présente des caractéristiques intrinsèques perturbées par les inhalations ;
 - une étape (E30) d'estimation d'une approximation ($\Delta U_{10_{TH}}(t)$, $U_{10_{TH}}(t)$)
 - 15 de ladite caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant (10) en l'absence d'inhalation pendant ladite période de fumage ;
 - une étape (E50) de calcul d'une intensité (F) des inhalations pendant ladite période de fumage à partir d'une intégration de la différence entre
 - 20 lesdites approximations pendant ladite période de fumage ; et
 - une étape (E60) d'estimation de ladite quantité de substrat vaporisée par l'élément chauffant au moins à partir de ladite intensité.
- 25 2. Procédé d'estimation selon la revendication 1, caractérisé en ce que la caractéristique de ladite tension ($U_{10}(t)$) à un instant donné est une variation ($\Delta U_{10}(t)$) de ladite tension à cet instant.
- 30 3. Procédé d'estimation selon la revendication 2, caractérisé en ce que l'approximation ($\Delta U_{10_{MES}}(t)$) de la variation de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant est calculée à partir de tensions ($U_{12}(t)$, $U_{11}(t)$) mesurées aux bornes d'au moins deux éléments, les tensions aux bornes de chacun desdits éléments donnant une approximation de la tension aux bornes dudit élément chauffant (10) à des instants
- 35 légèrement décalés dans le temps.

4. Procédé d'estimation selon la revendication 3, caractérisé en ce que lesdits éléments (11, 12) sont des circuits RC série connectés en série.

5 5. Procédé d'estimation selon la revendication 2, caractérisé en ce que l'approximation ($\Delta U_{10_MES}(t)$) de la variation de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant est la dérivée par rapport au temps d'une différence de potentiels mesurée aux bornes d'une résistance de mesure (R) connectée en série avec ledit élément chauffant (10).

10

6. Procédé d'estimation selon la revendication 1, caractérisé en ce que l'approximation de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant est la tension mesurée aux bornes d'une résistance de mesure (R) connectée en série avec ledit élément chauffant (10).

15

7. Cigarette électronique (1) comportant un élément chauffant (10) apte à vaporiser un substrat pendant une période de fumage, caractérisée en ce qu'elle comporte :

- 20 - des moyens (30) de mesure d'une approximation ($\Delta U_{10_MES}(t)$, $U_{10_MES}(t)$) d'une caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant (10) pendant cette période de fumage, ladite approximation étant mesurée aux bornes (B1, B2) d'un circuit (500) dont aucun composant ne présente des caractéristiques intrinsèques perturbées par les inhalations ;
- 25 - des moyens (30) d'estimation d'une approximation ($\Delta U_{10_TH}(t)$, $U_{10_TH}(t)$) de ladite caractéristique de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant (10) en l'absence d'inhalation pendant ladite période de fumage ;
- des moyens (30) de calcul d'une intensité (F) des inhalations pendant 30 ladite période de fumage à partir d'une intégration de la différence entre lesdites approximations pendant ladite période de fumage ; et
- des moyens (30) d'estimation de ladite quantité de substrat vaporisée par l'élément chauffant au moins à partir de ladite intensité.

35 8. Cigarette électronique selon la revendication 7, caractérisée en ce qu'elle comporte :

- au moins deux éléments, la tension aux bornes de chacun desdits éléments donnant une approximation de la tension aux bornes dudit élément chauffant (10) à des instants légèrement décalés dans le temps, et
 - 5 - des moyens pour mesurer une approximation ($\Delta U_{10_{MES}}(t)$) de la variation de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant à partir des tensions ($U_{12}(t)$, $U_{11}(t)$) mesurées aux bornes desdits éléments.
9. Cigarette électronique selon la revendication 8, caractérisé en
- 10 ce que lesdits circuits (11, 12) sont des circuits RC série connectés en série.
10. Cigarette électronique selon la revendication 6, caractérisé en
- 15 ce qu'elle comporte des moyens de calcul (30) aptes à mesurer une différence de potentiels aux bornes d'une résistance de mesure (R) connectée en série avec l'élément chauffant (10), et des moyens pour mesurer une approximation ($U_{10_{MES}}(t)$) de la variation de la tension ($U_{10}(t)$) aux bornes de l'élément chauffant à partir de ladite différence de potentiels.

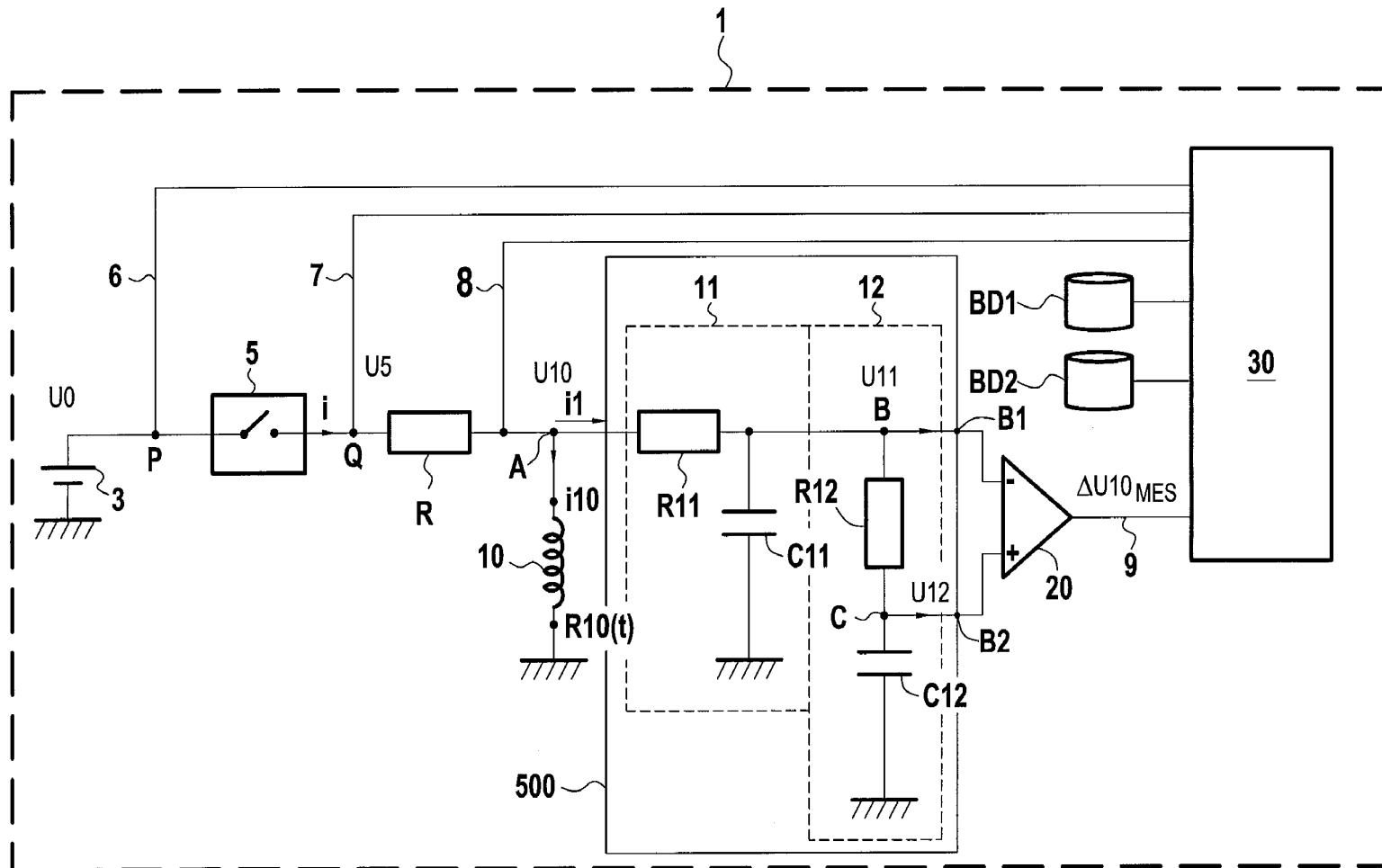


FIG.1

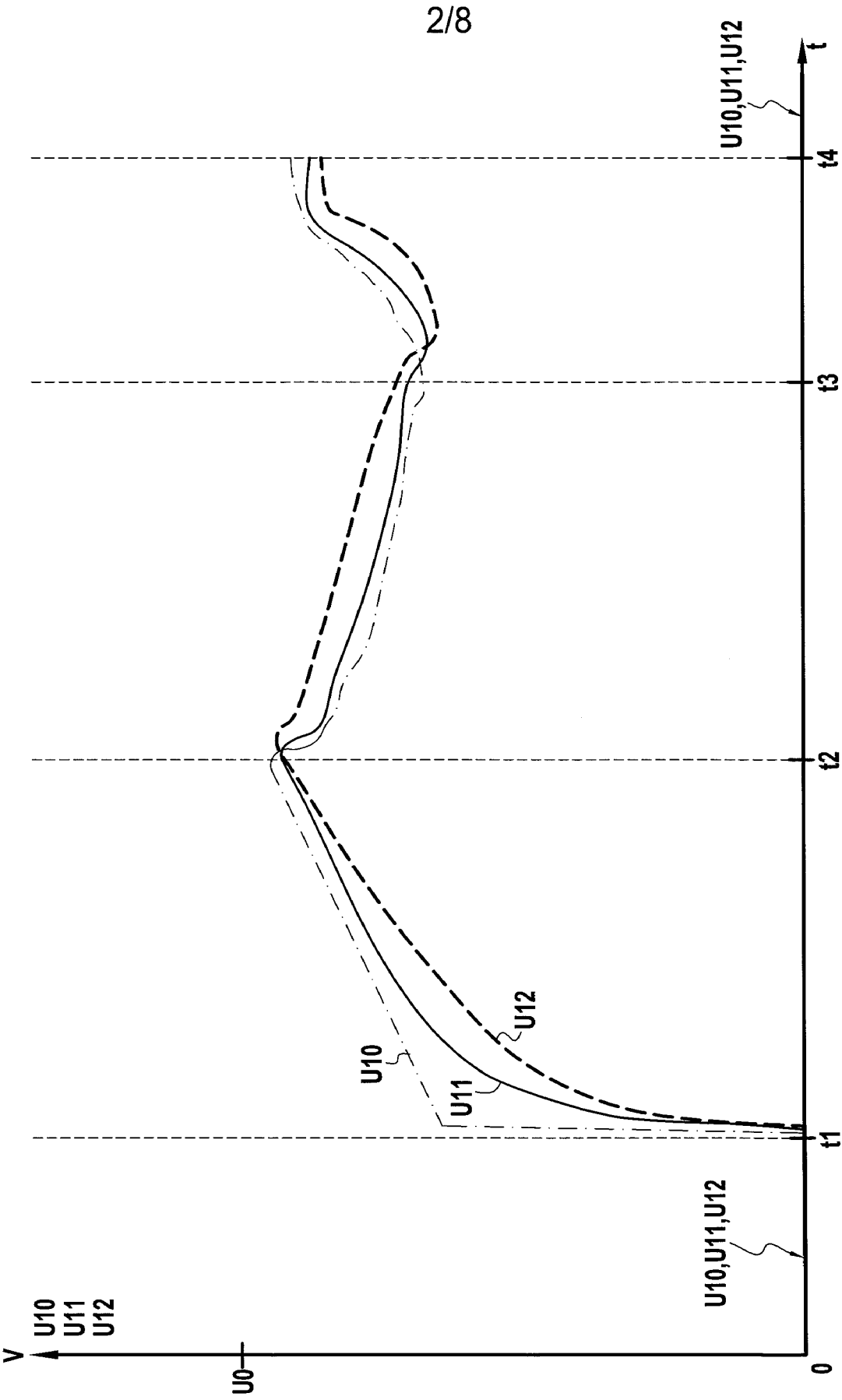


FIG.2

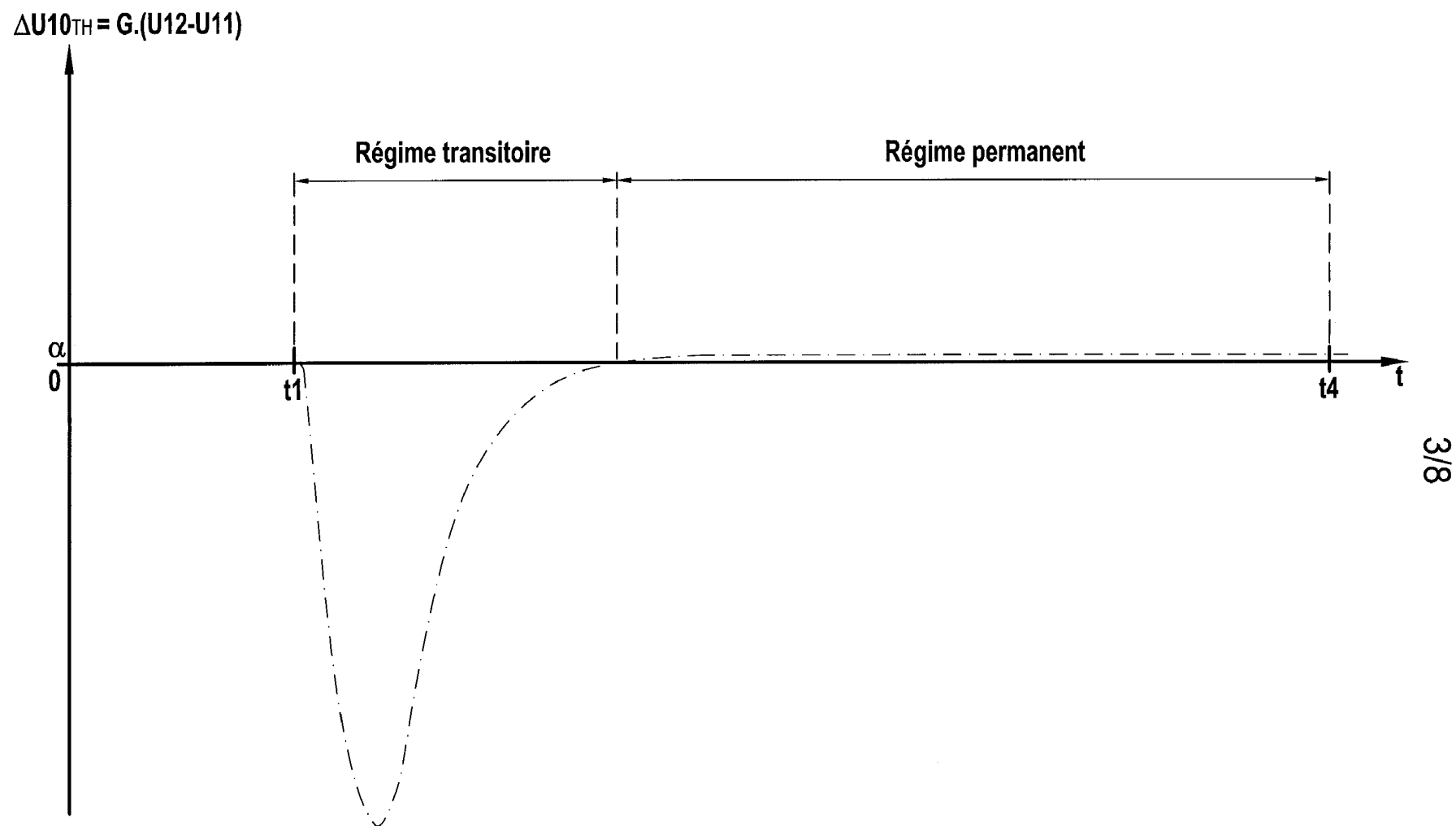


FIG.3

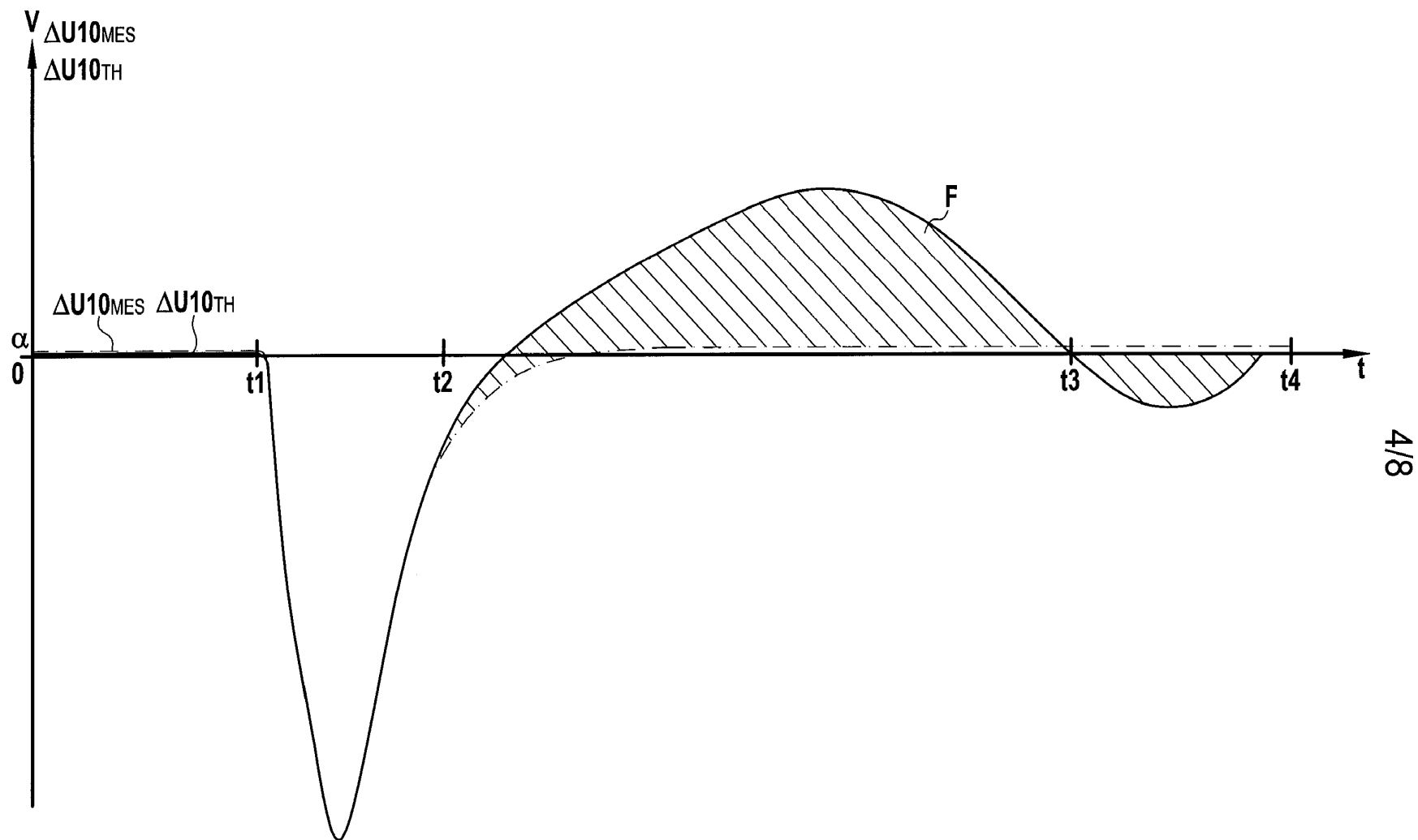


FIG.4

5/8

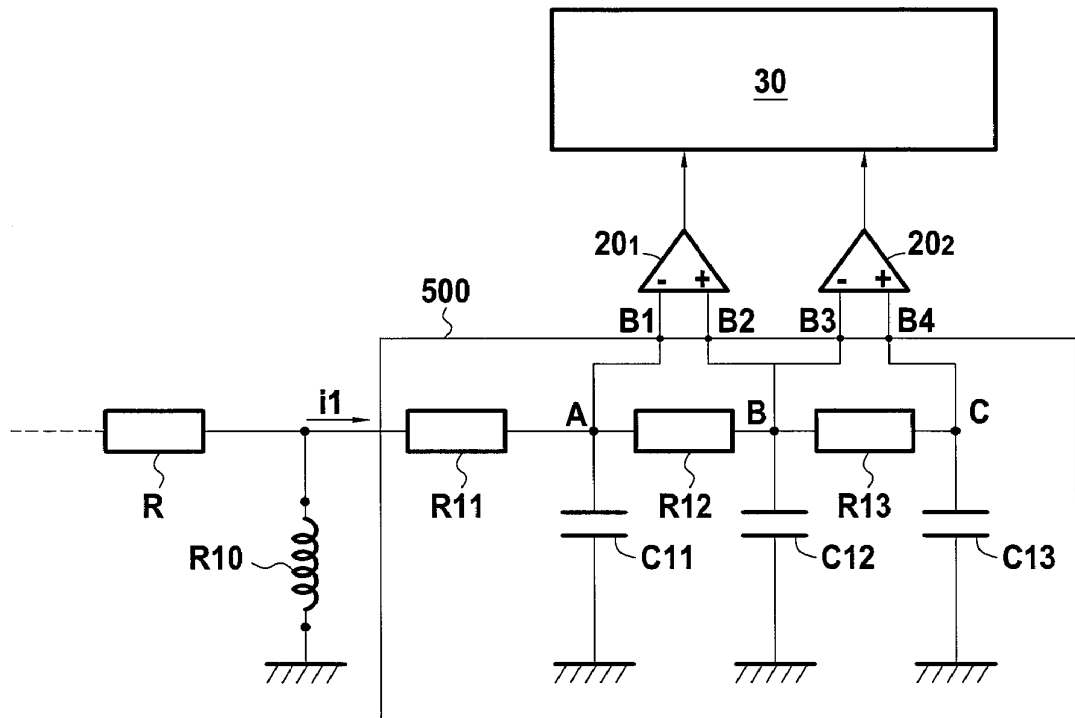


FIG.5

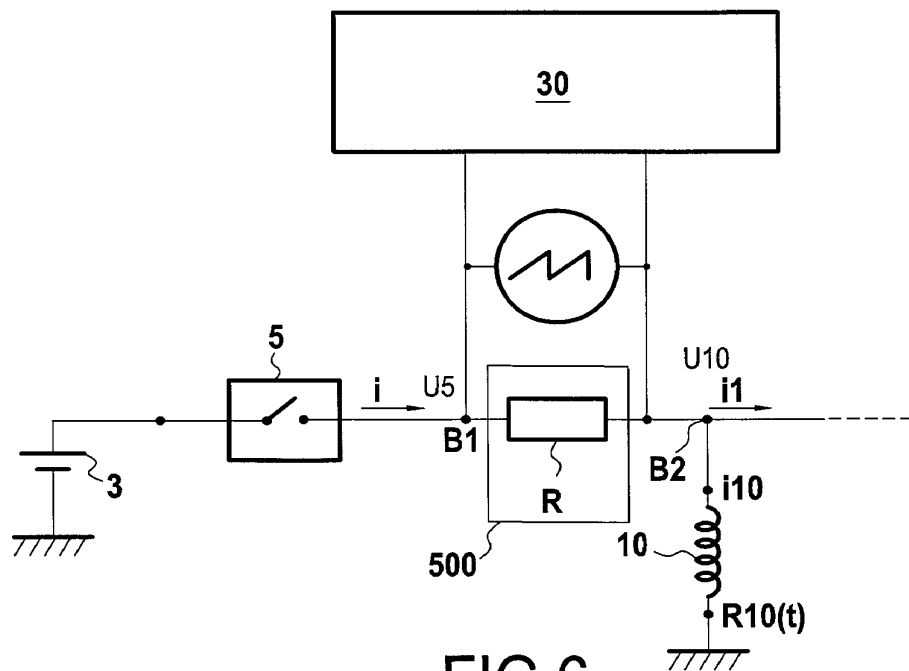


FIG.6

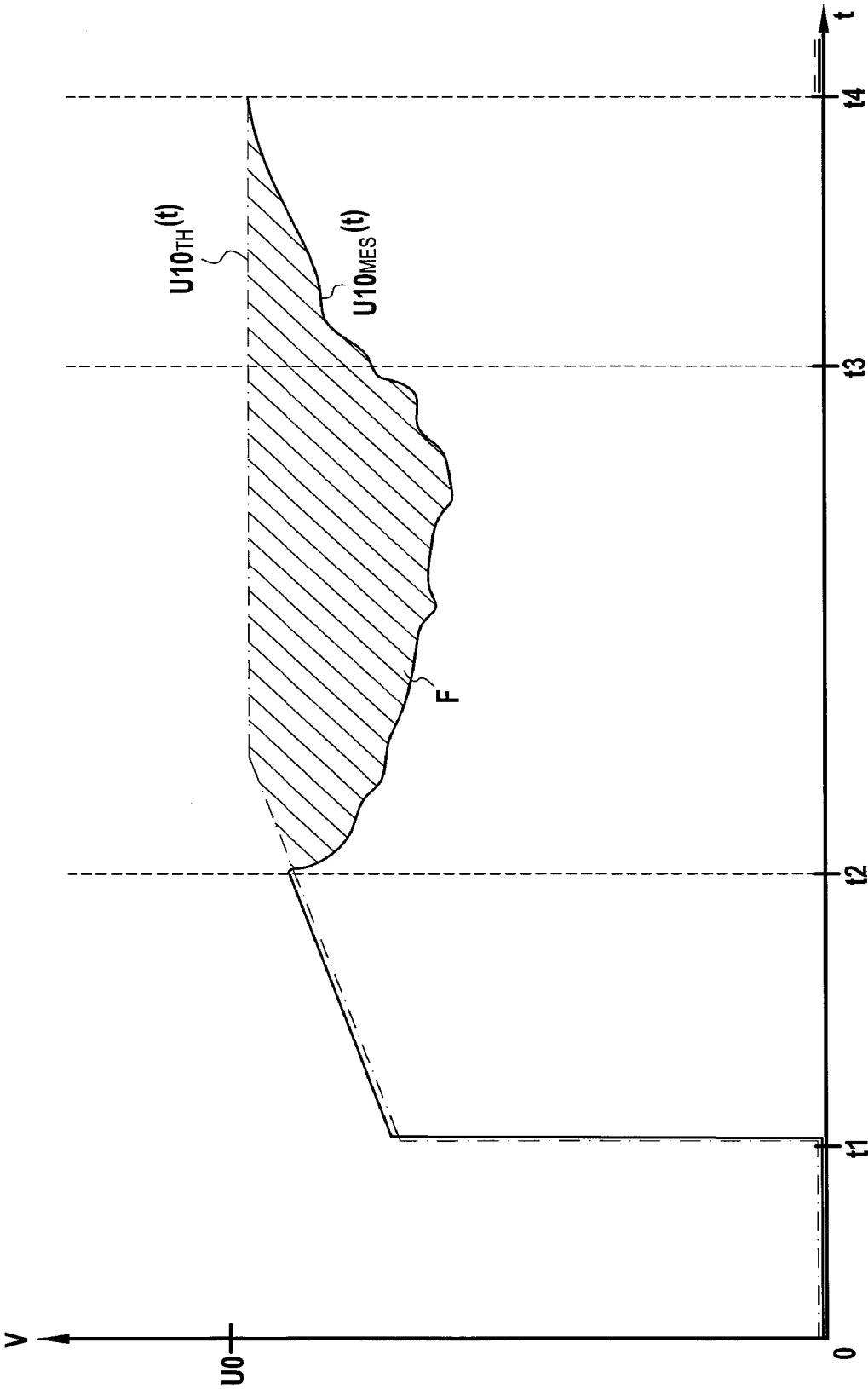


FIG.7

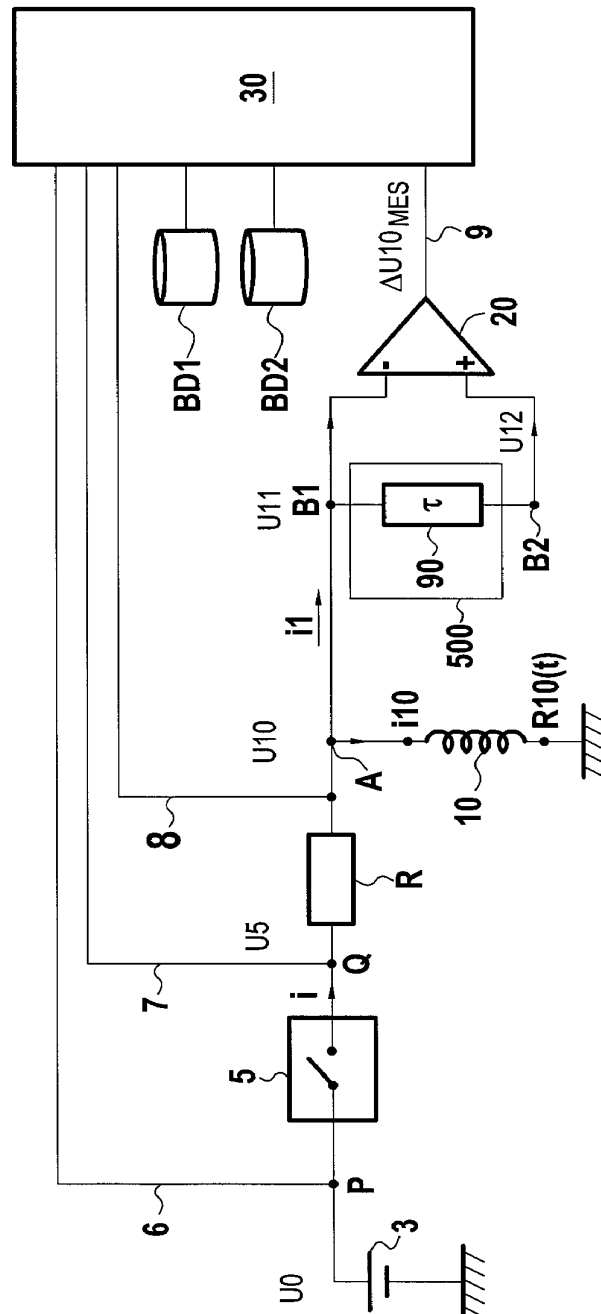


FIG. 8.

8/8

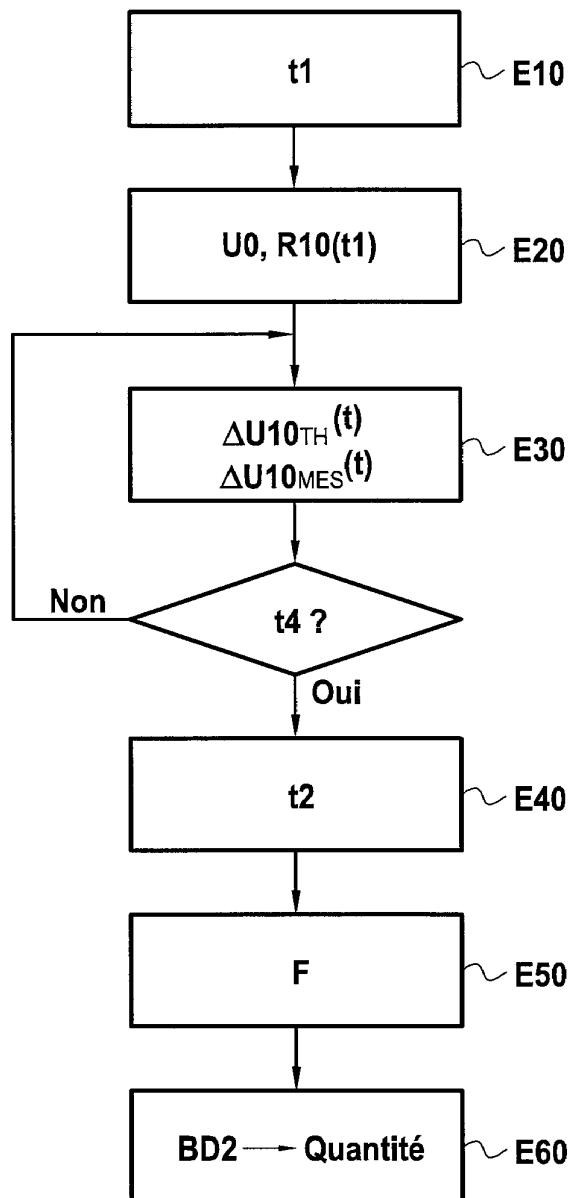


FIG.9

INTERNATIONAL SEARCH REPORT

International application No

PCT/FR2015/050416

A. CLASSIFICATION OF SUBJECT MATTER
 INV. G01N27/18 A24F47/00
 ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N A24F A61M H05B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 2 468 116 A1 (PHILIP MORRIS PROD [CH]) 27 June 2012 (2012-06-27)	1-3,7,8
A	figures 1-9 paragraphs [0045], [0046], [0069], [0075], [0080], [0081] -----	4-6,9,10
X	EP 2 143 346 A1 (PHILIP MORRIS PROD [CH]) 13 January 2010 (2010-01-13)	1,2,5-7, 10
A	figures 1-5 paragraphs [0001], [0006], [0007], [0025], [0069] -----	3,4,8,9
A	WO 2013/098398 A2 (PHILIP MORRIS PROD [CH]) 4 July 2013 (2013-07-04) figures 1-6 page 8, line 5 - page 10, line 2 page 17, line 1 - page 18, line 4 ----- -/-	1-10

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

30 April 2015

Date of mailing of the international search report

11/05/2015

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040,
 Fax: (+31-70) 340-3016

Authorized officer

Gangl, Martin

INTERNATIONAL SEARCH REPORT

International application No

PCT/FR2015/050416

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 430 566 A2 (PHILIP MORRIS [US] PHILIP MORRIS PROD [US]) 5 June 1991 (1991-06-05) figures 1-10 column 3, line 55 - column 4, line 53 column 5, line 31 - line 39 column 14, line 28 - line 58 -----	1-10
A	WO 2013/060781 A1 (PHILIP MORRIS PROD [CH]) 2 May 2013 (2013-05-02) page 3, line 19 - page 4, line 20; figures 1-5 page 17, line 1 - page 18, line 4 -----	1-10
A	US 6 040 560 A (FLEISCHHAUER GRIER S [US] ET AL) 21 March 2000 (2000-03-21) figures 1-19 column 2, line 61 - column 3, line 38 column 5, line 62 - column 6, line 11 column 9, line 38 - column 10, line 34 -----	1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/FR2015/050416

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 2468116	A1	27-06-2012	AU 2011347189 A1 11-07-2013
			CA 2822728 A1 28-06-2012
			CN 103338664 A 02-10-2013
			CO 6761317 A2 30-09-2013
			EA 201390963 A1 28-02-2014
			EP 2468116 A1 27-06-2012
			EP 2654470 A1 30-10-2013
			JP 2014501107 A 20-01-2014
			KR 20140004656 A 13-01-2014
			NZ 611897 A 30-01-2015
			SG 191276 A1 31-07-2013
			US 2013319435 A1 05-12-2013
			WO 2012085207 A1 28-06-2012

EP 2143346	A1	13-01-2010	AR 074040 A1 22-12-2010
			AU 2009267544 A1 14-01-2010
			CA 2729305 A1 14-01-2010
			CN 102088875 A 08-06-2011
			CO 6341532 A2 21-11-2011
			EG 25966 A 13-11-2012
			EP 2143346 A1 13-01-2010
			EP 2299855 A1 30-03-2011
			JP 5404779 B2 05-02-2014
			JP 2011527415 A 27-10-2011
			KR 20110025186 A 09-03-2011
			NZ 589885 A 25-10-2013
			RU 2011104185 A 20-08-2012
			TW 201007628 A 16-02-2010
			UA 100068 C2 12-11-2012
			WO 2010003480 A1 14-01-2010

WO 2013098398	A2	04-07-2013	AU 2012360820 A1 21-08-2014
			CA 2858479 A1 04-07-2013
			CN 103997921 A 20-08-2014
			EP 2797447 A2 05-11-2014
			HK 1198241 A1 20-03-2015
			JP 2015507477 A 12-03-2015
			KR 20140118985 A 08-10-2014
			US 2014345633 A1 27-11-2014
			WO 2013098398 A2 04-07-2013

EP 0430566	A2	05-06-1991	AT 120931 T 15-04-1995
			AU 642448 B2 21-10-1993
			AU 6762290 A 06-06-1991
			CA 2031227 A1 02-06-1991
			DE 69018577 D1 18-05-1995
			DE 69018577 T2 30-11-1995
			DK 0430566 T3 14-08-1995
			EP 0430566 A2 05-06-1991
			ES 2071045 T3 16-06-1995
			JP 3258657 B2 18-02-2002
			JP H03277265 A 09-12-1991
			NO 905151 A 03-06-1991
			TR 25309 A 01-01-1993
			US 5060671 A 29-10-1991

WO 2013060781	A1	02-05-2013	AR 088558 A1 18-06-2014
			AU 2012330370 A1 29-05-2014

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/FR2015/050416

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
		CA 2851933 A1	02-05-2013	
		CN 103889258 A	25-06-2014	
		EP 2770859 A1	03-09-2014	
		HK 1198106 A1	13-03-2015	
		JP 2014530632 A	20-11-2014	
		KR 20140094513 A	30-07-2014	
		US 2014299141 A1	09-10-2014	
		WO 2013060781 A1	02-05-2013	

US 6040560	A	21-03-2000	AT 284628 T	15-01-2005
			AU 743847 B2	07-02-2002
			AU 4901697 A	15-05-1998
			CA 2268657 A1	30-04-1998
			DE 69731980 D1	20-01-2005
			DE 69731980 T2	22-12-2005
			EP 0973419 A1	26-01-2000
			ES 2235229 T3	01-07-2005
			HK 1022080 A1	13-05-2005
			JP 3976345 B2	19-09-2007
			JP 2001502542 A	27-02-2001
			MX PA99003671 A	26-05-2005
			PT 973419 E	29-04-2005
			US 6040560 A	21-03-2000
			WO 9817131 A1	30-04-1998

A. CLASSEMENT DE L'OBJET DE LA DEMANDE
INV. G01N27/18 A24F47/00
ADD.

Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB

B. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE

Documentation minimale consultée (système de classification suivi des symboles de classement)

G01N A24F A61M H05B

Documentation consultée autre que la documentation minimale dans la mesure où ces documents relèvent des domaines sur lesquels a porté la recherche

Base de données électronique consultée au cours de la recherche internationale (nom de la base de données, et si cela est réalisable, termes de recherche utilisés)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie*	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
X	EP 2 468 116 A1 (PHILIP MORRIS PROD [CH]) 27 juin 2012 (2012-06-27)	1-3,7,8
A	figures 1-9 alinéas [0045], [0046], [0069], [0075], [0080], [0081] -----	4-6,9,10
X	EP 2 143 346 A1 (PHILIP MORRIS PROD [CH]) 13 janvier 2010 (2010-01-13)	1,2,5-7, 10
A	figures 1-5 alinéas [0001], [0006], [0007], [0025], [0069] -----	3,4,8,9
A	WO 2013/098398 A2 (PHILIP MORRIS PROD [CH]) 4 juillet 2013 (2013-07-04) figures 1-6 page 8, ligne 5 - page 10, ligne 2 page 17, ligne 1 - page 18, ligne 4 ----- -/-	1-10

☒ Voir la suite du cadre C pour la fin de la liste des documents

☒ Les documents de familles de brevets sont indiqués en annexe

* Catégories spéciales de documents cités:

"A" document définissant l'état général de la technique, non considéré comme particulièrement pertinent

"E" document antérieur, mais publié à la date de dépôt international ou après cette date

"L" document pouvant jeter un doute sur une revendication de priorité ou cité pour déterminer la date de publication d'une autre citation ou pour une raison spéciale (telle qu'indiquée)

"O" document se référant à une divulgation orale, à un usage, à une exposition ou tous autres moyens

"P" document publié avant la date de dépôt international, mais postérieurement à la date de priorité revendiquée

"T" document ultérieur publié après la date de dépôt international ou la date de priorité et n'appartenant pas à l'état de la technique pertinent, mais cité pour comprendre le principe ou la théorie constituant la base de l'invention

"X" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme nouvelle ou comme impliquant une activité inventive par rapport au document considéré isolément

"Y" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme impliquant une activité inventive lorsque le document est associé à un ou plusieurs autres documents de même nature, cette combinaison étant évidente pour une personne du métier

"&" document qui fait partie de la même famille de brevets

Date à laquelle la recherche internationale a été effectivement achevée

30 avril 2015

Date d'expédition du présent rapport de recherche internationale

11/05/2015

Nom et adresse postale de l'administration chargée de la recherche internationale
Office Européen des Brevets, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Fonctionnaire autorisé

Gangl, Martin

C(suite). DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie*	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
A	EP 0 430 566 A2 (PHILIP MORRIS [US] PHILIP MORRIS PROD [US]) 5 juin 1991 (1991-06-05) figures 1-10 colonne 3, ligne 55 - colonne 4, ligne 53 colonne 5, ligne 31 - ligne 39 colonne 14, ligne 28 - ligne 58 -----	1-10
A	WO 2013/060781 A1 (PHILIP MORRIS PROD [CH]) 2 mai 2013 (2013-05-02) page 3, ligne 19 - page 4, ligne 20; figures 1-5 page 17, ligne 1 - page 18, ligne 4 -----	1-10
A	US 6 040 560 A (FLEISCHHAUER GRIER S [US] ET AL) 21 mars 2000 (2000-03-21) figures 1-19 colonne 2, ligne 61 - colonne 3, ligne 38 colonne 5, ligne 62 - colonne 6, ligne 11 colonne 9, ligne 38 - colonne 10, ligne 34 -----	1-10

RAPPORT DE RECHERCHE INTERNATIONALE

Renseignements relatifs aux membres de familles de brevets

Demande internationale n°

PCT/FR2015/050416

Document brevet cité au rapport de recherche		Date de publication	Membre(s) de la famille de brevet(s)	Date de publication
EP 2468116	A1	27-06-2012	AU 2011347189 A1	11-07-2013
			CA 2822728 A1	28-06-2012
			CN 103338664 A	02-10-2013
			CO 6761317 A2	30-09-2013
			EA 201390963 A1	28-02-2014
			EP 2468116 A1	27-06-2012
			EP 2654470 A1	30-10-2013
			JP 2014501107 A	20-01-2014
			KR 20140004656 A	13-01-2014
			NZ 611897 A	30-01-2015
			SG 191276 A1	31-07-2013
			US 2013319435 A1	05-12-2013
			WO 2012085207 A1	28-06-2012

EP 2143346	A1	13-01-2010	AR 074040 A1	22-12-2010
			AU 2009267544 A1	14-01-2010
			CA 2729305 A1	14-01-2010
			CN 102088875 A	08-06-2011
			CO 6341532 A2	21-11-2011
			EG 25966 A	13-11-2012
			EP 2143346 A1	13-01-2010
			EP 2299855 A1	30-03-2011
			JP 5404779 B2	05-02-2014
			JP 2011527415 A	27-10-2011
			KR 20110025186 A	09-03-2011
			NZ 589885 A	25-10-2013
			RU 2011104185 A	20-08-2012
			TW 201007628 A	16-02-2010
			UA 100068 C2	12-11-2012
			WO 2010003480 A1	14-01-2010

WO 2013098398	A2	04-07-2013	AU 2012360820 A1	21-08-2014
			CA 2858479 A1	04-07-2013
			CN 103997921 A	20-08-2014
			EP 2797447 A2	05-11-2014
			HK 1198241 A1	20-03-2015
			JP 2015507477 A	12-03-2015
			KR 20140118985 A	08-10-2014
			US 2014345633 A1	27-11-2014
			WO 2013098398 A2	04-07-2013

EP 0430566	A2	05-06-1991	AT 120931 T	15-04-1995
			AU 642448 B2	21-10-1993
			AU 6762290 A	06-06-1991
			CA 2031227 A1	02-06-1991
			DE 69018577 D1	18-05-1995
			DE 69018577 T2	30-11-1995
			DK 0430566 T3	14-08-1995
			EP 0430566 A2	05-06-1991
			ES 2071045 T3	16-06-1995
			JP 3258657 B2	18-02-2002
			JP H03277265 A	09-12-1991
			NO 905151 A	03-06-1991
			TR 25309 A	01-01-1993
			US 5060671 A	29-10-1991

WO 2013060781	A1	02-05-2013	AR 088558 A1	18-06-2014
			AU 2012330370 A1	29-05-2014

RAPPORT DE RECHERCHE INTERNATIONALE

Renseignements relatifs aux membres de familles de brevets

Demande internationale n°

PCT/FR2015/050416

Document brevet cité au rapport de recherche	Date de publication	Membre(s) de la famille de brevet(s)	Date de publication	
		CA 2851933 A1	02-05-2013	
		CN 103889258 A	25-06-2014	
		EP 2770859 A1	03-09-2014	
		HK 1198106 A1	13-03-2015	
		JP 2014530632 A	20-11-2014	
		KR 20140094513 A	30-07-2014	
		US 2014299141 A1	09-10-2014	
		WO 2013060781 A1	02-05-2013	

US 6040560	A	21-03-2000	AT 284628 T	15-01-2005
			AU 743847 B2	07-02-2002
			AU 4901697 A	15-05-1998
			CA 2268657 A1	30-04-1998
			DE 69731980 D1	20-01-2005
			DE 69731980 T2	22-12-2005
			EP 0973419 A1	26-01-2000
			ES 2235229 T3	01-07-2005
			HK 1022080 A1	13-05-2005
			JP 3976345 B2	19-09-2007
			JP 2001502542 A	27-02-2001
			MX PA99003671 A	26-05-2005
			PT 973419 E	29-04-2005
			US 6040560 A	21-03-2000
			WO 9817131 A1	30-04-1998



- (51) International Patent Classification:
A24F 1/10 (2006.01)
- (21) International Application Number:
PCT/US2015/022299
- (22) International Filing Date:
24 March 2015 (24.03.2015)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/970,238 25 March 2014 (25.03.2014) US
14/483,828 11 September 2014 (11.09.2014) US
14/533,874 5 November 2014 (05.11.2014) US
- (71) Applicant: NICOTECH , LLC [US/US]; 20 River Terrace, Apt. 27E, New York, NY 10282 (US).
- (72) Inventors: SPINKA, Kristofer; 20 River Terrace, Apt. 27E, New York, NY 10282 (US). SPINKA, Xabay; 20 River Terrace, Apt. 27E, New York, NY 10282 (US).
- (74) Agent: KING, Jonathan, R.; Blank Rome LLP, 600 New Hampshire, NW, Washington, DC 20037 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: INHALATION SENSOR FOR ALTERNATIVE NICOTINE/THC DELIVERY DEVICE

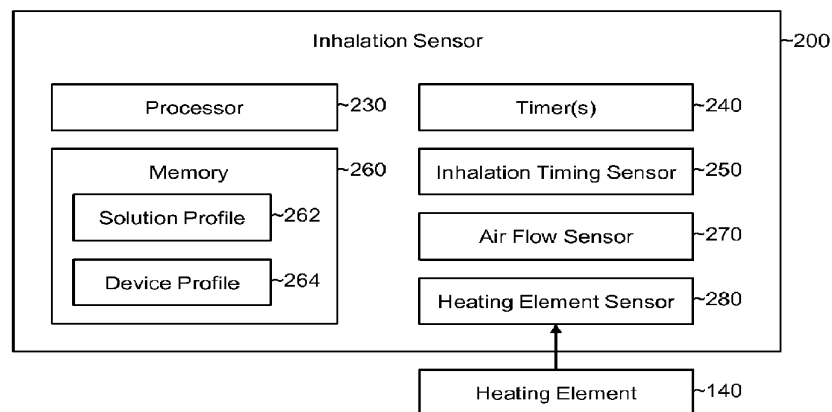


FIG. 2

(57) **Abstract:** An inhalation sensor for an alternative nicotine or THC delivery device having a diluted nicotine or THC solution. The inhalation sensor includes a processor and memory. The memory includes a solution profile including information indicative of the nicotine or THC concentration of the diluted nicotine or THC solution and a device profile including information indicative of the alternative nicotine or THC delivery device. The inhalation sensor is configured to determine an amount of nicotine or THC consumed by a user of the alternative nicotine or THC delivery device based on the solution profile and the device profile.

INHALATION SENSOR FOR ALTERNATIVE NICOTINE/THC DELIVERY DEVICE**CROSS REFERENCE TO RELATED APPLICATION**

[0001] This application claims priority to U.S. Application No. 14483828, filed September 11, 2014, and U.S. Provisional Application No. 61/970,238, filed March 25, 2014, the entire contents of which is incorporated herein by reference.

BACKGROUNDField of the Invention

[0002] This disclosure relates to an inhalation sensor configured to determine and/or regulate an amount of nicotine and/or tetrahydrocannabinol (THC) delivered by the alternative nicotine/THC delivery device.

Background of the Invention

[0003] Alternative nicotine delivery devices (such as electronic cigarettes, vaporizers, and tobacco furnaces) are a widely popular means of nicotine delivery. Because they are more analogous to traditional cigarettes than other nicotine delivery devices like gums or patches, it is easier for most users to transition from traditional cigarettes to alternative nicotine delivery devices.

[0004] Traditional cigarettes, by way of the smoke itself, create a self-limiting maximum rate of nicotine consumption because inhaling traditional cigarette smoke at an increased rate creates levels of discomfort (for example, coughing, carbon monoxide, heat from the smoke, etc.). The alternative nicotine delivery device, however, poses a risk of increased nicotine consumption because the almost-sensationless effect of inhaling the vaporized nicotine solution does not have the self-limiting side effects of traditional cigarettes. Due to inconsistency in manufacturing, the amount of nicotine delivered by each alternative nicotine delivery device may vary from unit to

unit. Therefore, nicotine consumption per alternative nicotine delivery device cannot be reliably tracked.

[0005] Inhalation of THC is being decriminalized and/or legalized in an increasing number of jurisdictions. Similar to nicotine, THC may be inhaled by an alternative delivery device which does not produce the self-limiting side effects of traditional cigarette.

SUMMARY

[0006] One embodiment of the present invention is an inhalation sensor for an alternative nicotine/THC delivery device having a diluted nicotine/THC solution. The inhalation sensor includes a processor and memory. The memory includes a solution profile including information indicative of the nicotine/THC concentration of the diluted nicotine/THC solution and a device profile including information indicative of the alternative nicotine/THC delivery device. The inhalation sensor is configured to determine an amount of nicotine/THC consumed by a user of the alternative nicotine/THC delivery device based on the solution profile and the device profile.

[0007] In some instances, the simple act of informing the user regarding nicotine/THC consumption may reduce the nicotine/THC consumption of the user. In other instances, the user may want to be restricted from exceeding a predetermined maximum nicotine/THC consumption level. Accordingly, the alternative nicotine/THC delivery device may restrict the amount of nicotine/THC consumed by the user based on a predetermined nicotine/THC consumption amount or user input.

[0008] Exemplary embodiments of the present invention may enable an alternative nicotine delivery device to be classified as a smoking cessation device rather than a simple nicotine delivery system. This classification may enable the alternative nicotine delivery device to be purchased through health insurance providers and/or avoid the burdens of additional regulation.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] Exemplary embodiments will be set forth with reference to the drawings, in which:

[0010] FIG. 1A illustrates an alternative nicotine/THC delivery device according to an exemplary embodiment of the present invention;

[0011] FIG. 1B illustrates an alternative nicotine/THC delivery device according to another exemplary embodiment of the present invention;

[0012] FIG. 1C illustrates an alternative nicotine/THC delivery device according to another exemplary embodiment of the present invention;

[0013] FIG. 2 illustrates an inhalation sensor according to an exemplary embodiment of the present invention;

[0014] FIG. 3 illustrates an alternative nicotine/THC delivery device according to another exemplary embodiment of the present invention;

[0015] FIG. 4 illustrates an alternative nicotine/THC delivery device according to yet another exemplary embodiment of the present invention;

[0016] FIG. 5 illustrates an alternative nicotine/THC delivery device according to yet another exemplary embodiment of the present invention;

[0017] FIG. 6 illustrates an alternative nicotine/THC delivery device according to yet another exemplary embodiment of the present invention; and

[0018] FIG. 7 illustrates another view of the charging unit illustrated in FIG. 1B and/or the charging unit illustrated in FIG. 1C according to an exemplary embodiment of the present invention.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

[0019] Exemplary embodiments of the present invention will be set forth in detail with reference to the accompanying drawings, in which like reference numerals refer to like elements throughout. The description set forth below and illustrated in part by the drawings is intended to serve as a description of exemplary embodiments of the application and is not intended to represent the only methods by which the present application can be constructed and/or utilized. The description sets forth the functions and the sequence of steps for constructing, calibrating and operating exemplary embodiments of the present invention. It is to be understood, however, that the same or equivalent functions and sequences can be accomplished by different embodiments that are also intended to be encompassed within the spirit and scope of this disclosure. Exemplary embodiments illustrated in the accompanying drawings are not necessarily to scale and are instead provided to convey the inventive concepts to one of ordinary skill in the art.

[0020] FIG. 1A illustrates an alternative nicotine/THC delivery device 100a, including a reservoir 110a for storing a diluted nicotine/THC solution 112, a power source 120a, electronic circuitry 130a, and a heating element 140 (shown inside cut-out 150). The device 100a may also include a negative pressure switch or manually actuated switch (not shown). The electronic circuitry 130a may include a processor and may be configured to electrically connect the power source 120a and the heating element 140 to vaporize the solution 112 in response to the switch. The electronic circuitry 130a may also provide very basic functions including passing current to a decorative light emitting diode (LED), regulating electrical current flow to the heating element 140, and limiting the contiguous amount of time the heating element 140 can be in use for one inhalation (*i.e.*, draw, usage, puff) of the device in order to protect the solution 112 and heating

element 140 from overheating and releasing toxic substances from the nicotine/THC solution (e.g., formaldehyde).

[0021] While the device 100a may be an electronic cigarette including the reservoir 110a for storing a diluted nicotine/THC solution 112, in another exemplary embodiment the device 100a may be any other vaporizing device configured to deliver any vaporized solution (with or without nicotine or THC). In yet another exemplary embodiment, the 100 may be a tobacco furnace including a nicotine/THC cartridge (for example, a cartridge containing tobacco or cannabis and a filter) in addition to or instead of the reservoir 110a for storing the solution 112.

[0022] The reservoir 110a may be refillable or disposable. The power source 120a may be a battery, a fuel injector, or any other device configured to supply power to the heating element 140. The power source 120a may be rechargeable or disposable. The power source 120a may be configured to recharge via a wired or wireless connection, by mating with a charging unit as discussed below, and/or by harvesting power from sources such as radio waves, heat, light, motion, etc. The reservoir 110 may be removably connected to the power source 120a or the reservoir 110a and the power source 120a may be integrated into a single device. The electronic circuitry 130a may be incorporated as part of the power source 120a, the reservoir 110a or as a separate, removably connectable device.

[0023] FIG. 1B illustrates an alternative nicotine/THC delivery device 100b according to another exemplary embodiment of the present invention. The device 100b may include one or more inhalation units 110b and a charging unit 180a. Similar to the device 100a, the inhalation units 110b may include a reservoir for storing a diluted nicotine/THC solution 112, a power source, and a heating element to vaporize the solution 112.

[0024] The charging unit 180a may include a power source 120b, electronic circuitry 130b, and memory 160. The power source 120b may be configured to store and transfer power to the power source of the inhalation units 110b. For example, the power source of the inhalation unit 110b may be a rechargeable battery and the power source 120b (which may also be a rechargeable battery) may store electric power and charge and recharge the battery of one or more of the inhalation units 110b when one or more of the inhalation units 110b is coupled with the charging unit 180a.

[0025] The memory 160 may be any suitable device configured to store data. For example, the memory 160 may be non-volatile memory. The electronic circuitry 130b may include a processor (similar to the electronic circuitry 130a).

[0026] FIG. 1C illustrates an alternative nicotine/THC delivery device 100c according to another exemplary embodiment of the present invention. The device 100c may include a compressed air inhalation unit 110c and a charging unit 180b. Similar to the charging unit 180a, the charging unit 180b may include a power source 120b, electronic circuitry 130b, and memory 160.

[0027] The charging unit 180b may include a compressed nicotine/THC vapor reservoir 170 configured to store the nicotine/THC solution 112 under pressure. Unlike the inhalation unit 110b, the inhalation unit 110c may not include a power source or a heating element. Instead, the device 100c may be configured such that the reservoir 170 fills and/or refills the compressed air inhalation units 110c with a pressurized nicotine/THC solution 112 when the compressed air inhalation unit 110c mates with the charging unit 180b. In this instance, the compressed air inhalation unit 110c is configured to deliver the pressurized solution 112 to the user in response to an inhalation.

[0028] FIG. 2 illustrates an inhalation sensor 200 according to an exemplary embodiment of the present invention. The inhalation sensor 200 includes a processor 230, at least one timer 240, and memory 260. The memory 260 may include a solution profile 262 and a device profile 264. The inhalation sensor 200 may also include an inhalation timing sensor 250, an air flow sensor 270, and/or a heating element sensor 280.

[0029] The processor 230 may be an integrated circuit or soft logic processor. The memory 260 may be any non-transitory computer-readable storage medium, such flash memory, configured to store data and instructions that, when executed by the processor 230, carry out relevant portions of the features described herein.

[0030] The timer(s) 240 may be any device configured to measure time intervals. Each of the one or more timers 240 may be “always on” (real-time clock) and measure time intervals as long as the device 100a-c is connected to a power source or the device 100a-c may include a switch to connect and disconnect power to one or all of the timers 240. In either instance, the timer or timers 240 may be configured to measure time intervals both during and after an inhalation of the device 100a-c.

[0031] The inhalation timing sensor 250 may be any device configured to determine if a user is actively inhaling the solution 112. The inhalation timing sensor 250 may be configured to detect, for example, the output of the negative pressure switch described above, negative pressure from the user, air flow, flow of the solution 112 from the reservoir 110a, etc. The air flow may be determined by an optional air flow sensor 270 (discussed below).

[0032] As described in more detail below, the inhalation sensor 200 may be incorporated within the device 100a, the inhalation unit 110b, the charging unit 180, an external device, or any

combination thereof. In one example, the inhalation sensor 200 may be incorporated within the device 100a (for example, as part of the electronic circuitry 130a).

[0033] In another example, the inhalation sensor 200 may be incorporated within the device 100b. In this example, the memory 160 may include the memory 260; the electronic circuitry 130b may include the processor 230 and a timer 240; and the inhalation unit 110b may include a timer 240, the inhalation timing sensor 250, the air flow sensor 270 and/or the heating element sensor 280. In this example, the electronic circuitry 130b and the inhalation unit 110b may include communications circuitry configured to send and receive data between the electronic circuitry 130b and the inhalation unit 110b. The communications between the electronic circuitry 130b and the inhalation unit 110b may be via wired connection configured to transfer data when the inhalation unit 110b is paired with the charging unit 180 or wireless connection (*e.g.*, Bluetooth, near field communication, etc.)

[0034] In another example, the inhalation sensor 200 may be wholly or partially incorporated within an external device (*e.g.*, a computer, a smart phone, a smart watch, a fitness tracker, etc.). In this example, the external device may include the processor 230, the memory 260, the timer 240; and the device 100a-c may include the inhalation timing sensor, the air flow sensor, and/or the heating element sensor. The external device and the device 100a-c may include wired or wireless communications circuitry as described above.

[0035] The inhalation sensor 200 is configured to determine (*i.e.*, estimate and/or measure) the amount of nicotine or THC consumed by a user. One factor used to determine the amount of nicotine or THC consumed by a user is the nicotine/THC content of the solution 112. The nicotine/THC content of the solution 112 may be pre-determined (for example, by analyzing the solution 112 with a spectrometer tank) and stored in the memory 260 of as part of the solution

profile 262. The solution profile 262 may also include additional information regarding the solution 112. For example, the solution profile 262 may include the burning point of the solution 112 (*i.e.*, the temperature at which the solution 112 begins releasing toxic substances to the user).

[0036] In one exemplary embodiment, the device 100a-c may be configured to pair with a single diluted nicotine/THC solution 112 (*e.g.*, a single use electronic cigarette, an electronic cigarette with one type of mechanically compatible reservoir 110a pre-filled with a single type of solution 112, etc.). In this embodiment, the solution profile 264 associated with the solution 112 may be pre-stored in the memory 260 of the inhalation sensor 200.

[0037] In another exemplary embodiment, the device 100a-c may be configured to pair with a multiple diluted nicotine/THC solutions 112 (*e.g.*, an electronic cigarette with multiple compatible reservoirs 110a, a refillable vaporizer, etc.). In this embodiment, the solution profile 262 may be selected by the user based on the solution 112 paired with the device 100a-c. The solution profile 262 associated with the solution 112 may be downloaded from the internet via an external device (*e.g.*, a computer, a smart phone, etc.) and transferred to the inhalation sensor 200 via a wired (*e.g.*, USB) or wireless connection (*e.g.*, Bluetooth). The solution profile 262 associated with the solution 112 may be determined and/or distributed by the manufacturer of the solution 112 or a third party (for example, NicoTech, LLC).

[0038] The amount of nicotine or THC consumed by a user may be further based on the type of solution 112 (*e.g.*, a vegetable glycerin solution, a propylene glycol solution, etc.). Accordingly, the solution profile 262 may include information indicative of the solution type and the inhalation sensor 200 may further determine the amount of nicotine or THC consumed by the user based on the solution type.

[0039] In instances where the device 100a-b includes a heating element 140, another factor used to determine the amount of nicotine or THC consumed by a user may be the temperature of the heating element 140. After the heating element 140 is activated during inhalation, the temperature of the heating element 140 rises. Accordingly, the temperature of the heating element 140 is dependent on the length of an inhalation. Accordingly, the inhalation sensor 200 may be configured to determine information indicative of the temperature of the heating element 140 based on the length of an inhalation.

[0040] The inhalation sensor 200 may determine the length of each inhalation based on the output of the inhalation timing sensor 250 and the timer 240 which may be incorporated, for example, in the device 100a or the inhalation unit 112b. For example, the inhalation timing sensor 250 may output signals indicative of the beginning and end of an inhalation and the inhalation sensor 200 may determine the elapsed time between the beginning and the end of the inhalation based on the output of the timer 240.

[0041] The relationship between the length of an inhalation and the temperature of the heating element 140 may be pre-determined (for example, by simulating the use of a prototypical alternative nicotine/THC delivery device and measuring the physical characteristics of the device) and stored in the memory 260 as part of the device profile 264. The device profile 264 may be determined, for example, by placing the a prototypical alternative nicotine/THC delivery device (*e.g.*, the same model as the alternative nicotine/THC delivery device 100a-b that includes the inhalation sensor 200) in a simulated puffing device, activating the prototypical alternative nicotine/THC delivery device for a series of successive durations and measuring the temperature of the heating element 140. The device profile 264 may also include addition information regarding the device 100a-c. The additional information may be pre-determined using the

simulated puffing device in combination with the spectrometer, a gas chromatograph, a volume measurement setup, etc. For example, the device profile 264 may determine if and when the device 100a-b reaches the burning point of the solution 112.

[0042] The temperature of the heating element 140 may also be dependent on the time elapsed between each inhalation. As described above, some devices limit the length of a single inhalation in order to prevent the heating element 140 from overheating and burning the solution 112. A user, however, may initiate multiple inhalations in quick succession, activating the heating element 140 before it has cooled down after the initial inhalation. Therefore, the amount of nicotine or THC consumed by the user may be further based on the time between inhalations. Accordingly, the inhalation sensor 200 may be further configured to determine the amount of nicotine or THC consumed by the user further based on the time between inhalations. Similar to the duration of each inhalation, the time between inhalations may be determined based on the output of the timer 240 and the inhalation timing sensor 250.

[0043] The inhalation sensor 200 may determine the information indicative of the temperature of the heating element 140 based on the duration of each inhalation, the time between inhalations, and information included in the device profile 254. For example, the device profile 264 may include a ramp up profile indicative of the temperature of the heating element 140 during ramp up (*i.e.*, the temperature increase of the heating element 140 during inhalation) and a decaying profile indicative of the temperature of the heating element 140 during ramp down (*i.e.*, the temperature decrease of the heating element 140 after the heating element is de-activated). Accordingly, the inhalation sensor 200 may be configured to determine information indicative of the temperature of the heating element 140 during a single inhalation or multiple successive inhalations based on the duration of each inhalation and the time elapsed between inhalations.

[0044] Instead of relying solely on the device profile 264, the inhalation sensor 200 may include an optional heating element sensor 280 incorporated in the device 100a or the inhalation unit 110b. The heating element sensor 280 may be configured to determine the temperature of the heating element 140, for example, based on the in-line resistance and voltage of the heating element 140 detected by the heating element sensor 280.

[0045] The amount of nicotine or THC consumed by a user may also depend on the air flow rate of the device 100a or inhalation unit 100b during each inhalation. The inhalation sensor 200 may estimate the air flow during each inhalation based on information included in the device profile 264. For example, an estimated air flow rate may be pre-determined by simulating the use of a prototypical device as described above and measuring the air flow of the prototypical device during one or more simulated inhalations. In this example, the inhalation sensor 200 may estimate the air flow during each inhalation, for example, by multiplying the estimated air flow rate by the duration of each inhalation. Alternatively, the inhalation sensor 200 may include an optional air flow sensor 270. The air flow sensor 270 may be incorporated within the device 100a or the inhalation unit 110b and may be configured to determine the air flow or air flow rate of the device 100a-b during each inhalation. The air flow sensor 270 may be any device configured to measure or estimate the air flow or air flow rate of the device 100a or the inhalation unit 100b, including a pressure gauge, a vacuum gauge, a diaphragm, an impeller setup, etc.

[0046] As described above, continuing to inhale from the device 100a-b after the temperature of the heating element 140 has reached the burning point of the solution 112 may cause the user to ingest potentially toxic substances (*e.g.*, formaldehyde) from the solution 112. Conventional alternative nicotine/THC delivery devices may attempt to prevent the burning of a nicotine/THC

solution by limiting the duration of a single inhalation. A user, however, may further increase the temperature of a heating element of a conventional alternative nicotine/THC delivery device by initiating multiple successive inhalations. As also described above, the inhalation sensor 200 of the present invention may be configured to determine the temperature of the heating element 140 and the solution profile 262 may include information indicative of the boiling point of the solution 112. Therefore, the inhalation sensor 200 may be further configured to prevent the heating element 140 from boiling the solution 112 (even when the user initiates successive inhalations) by comparing the temperature of the heating element 140 (as determined by the inhalation sensor 200) and the boiling point of the solution 112 and outputting a signal if the temperature of the heating element 140 is approaching or exceeds the boiling point of the solution 112. The device 100a-b may be configured to prevent the heating element 140 from approaching or exceeding the boiling point of the solution 112 (*e.g.*, by disconnecting the heating element 140 from the power source 120) and/or output an audible or visual warning (*e.g.*, via an LED or speaker) to the user if the temperature of the heating element 140 is approaching or exceeds the boiling point of the solution 112.

[0047] The inhalation sensor 200 may be further configured to determine (*i.e.*, estimate or measure) the nicotine, cotinine, or THC levels of a user. Because nicotine and THC are metabolized primarily by liver enzymes, the nicotine, cotinine, or THC levels of a user may be further based on the liver performance of the user. Accordingly, the inhalation sensor 200 may be further configured to estimate the liver performance of the user based on static and/or dynamic biometrics of the user stored, for example, in the memory 260. The static biometrics of the user may include the body weight of the user (which may be used as an estimate of liver mass) and/or the sex, age, height, weight, and/or body type of the user (which may be used as an

estimate of liver performance). The static biometrics of the user may also include the user's average water/fluid intake, sampled cotinine levels, sampled hormone levels, etc. The static biometrics of the user may be input into the inhalation sensor 200 directly or input into an external device (*e.g.*, a computer, a smart phone, etc.), transferred to the inhalation sensor 200 via a wired or wireless connection.

[0048] The dynamic biometrics of the user may include the metabolic rate of the user. The user's metabolic rate may be determined by an external device (*e.g.*, a fitness tracker, a fitness watch, etc.) and transferred to and stored by the inhalation sensor 200 as described above. The dynamic biometrics of the user may also include hydration of the user. The user's hydration may be similarly determined by an external device and transferred to the inhalation sensor 200. Alternatively, the device 100a-c may include a hydration sensor. For example, the hydration sensor may be located on the exterior surface of the device 100a or inhalation unit 110b-c and may determine the bioelectrical impedance of the user based on contact with the user's fingers or mouth. In this instance, the inhalation sensor 200 may estimate the user's hydration based on the bioelectrical impedance of the user.

[0049] As described above, the inhalation sensor 200 may be integrated with the device 100a-c and may be configured to receive static and/or dynamic biometrics of the user from an external device. Alternatively, the inhalation sensor 200 may be stored and executed by an external device configured to receive the duration of each inhalation, the time between inhalations, and/or the bioelectrical impedance of the user from the device 100a-b.

[0050] The ramp up profile and the decaying profile of the device 100a-c may change over time. For example, the heating element 140 may oxidize or the output of the power supply 120a-b may change. Accordingly, the inhalation sensor 200 may be configured to update the device profile

264 to account for the changing characteristics of the device 100a-c. For example, the inhalation sensor 200 may be configured to receive measurements or estimates of the nicotine, cotinine, or THC levels of a user (*e.g.*, from an external device as described above) and update the device profile 264 based on the measured or estimated nicotine, cotinine, or THC levels of a user in order to more accurately determine the amount of nicotine or THC consumed by a user and/or the nicotine, cotinine, or THC levels of the user.

[0051] In another low-cost exemplary embodiment of the present invention, the device 100a-b may include a capacitor and the power source 120a. The power source 120a is configured to charge the capacitor. The capacitor in turn provides power to the heating element 140 for one session. In this instance, because the amount of power stored by the capacitor and delivered to the heating element 140 is predetermined, the amount of nicotine or THC consumed by a user may be pre-determined and stored in the inhalation sensor 200. Furthermore, the circuit may be arranged such that the capacitor is trickle-charged (charged slowly) from the power source 120a at a rate inverse to the half-life of nicotine or THC. Accordingly, as the concentration of nicotine or THC in the user falls, the capacitor's charge increases and allows the user to consume more nicotine or THC only as the concentration of nicotine or THC in the user falls. This embodiment provides a low-cost alternative to a realtime clock with digital logic while limiting the rate at which a user may consume nicotine or THC over time.

[0052] In embodiments where the inhalation unit 110c does not include a heating element (for example, as shown in FIG. 1C), the inhalation sensor 200 may be realized in a device external to the inhalation unit 110c (for example, the charging unit 180b or an external device) and may be configured to determine the amount of nicotine or THC consumed by the user based on the

solution profile 262, the device profile 264, and the time intervals between each instance when the inhalation unit 110c is refilled by the reservoir 170.

[0053] For example, the solution profile 262 may include the nicotine or THC concentration information as described above and the device profile 264 may include information indicative of the amount of vapor stored in the inhalation unit 110c. Each time the inhalation unit 110c is refilled by the reservoir 170, the inhalation sensor 200 may assume that the inhalation included the amount of vapor stored in the inhalation unit 110c. In this instance, the inhalation sensor 200 may estimate that the inhalation took place at some time between when the inhalation unit 110c was disconnected and reconnected with the charging unit 180b.

[0054] Alternatively, the inhalation unit 110c may contain a small power source (*e.g.*, a battery a rapid charge capacitor, etc.) that is recharged when the inhalation unit 110c is inserted into the reservoir 170. In this instance, the inhalation unit 110c may be configured to determine the time of the inhalation and may transfer information indicative of the inhalation time to the charging unit 180b when the inhalation unit 110c mates with the charging unit 180b.

[0055] The inhalation sensor 200 may be configured to output the nicotine/THC consumption information (*e.g.*, the amount of nicotine or THC consumed by the user and/or user nicotine, cotinine, or THC levels) to the user in the form of visual or audible notification and/or output the nicotine/THC consumption information to an external device (*e.g.*, a computer, a smart phone, a fitness tracker, a fitness watch, etc.).

[0056] FIG. 3 illustrates an alternative nicotine/THC delivery device 300 according to an exemplary embodiment of the present invention. The device 300 may be configured to deliver the nicotine/THC solution 112 similar to the device 100a or inhalation unit 110b-c. The device 300 may also include visual indicators 310, 320, and 330 configured to output the nicotine/THC

consumption information described above. As described in more detail below, the visual indicator 310, 320, and 330 may be any suitable device configured to selectively emit or reflect light. In the exemplary embodiment illustrated in FIG. 3, a plurality of visual indicators 310 emit or reflect light proportional to the nicotine or THC consumption over a predetermined time period or user nicotine, cotinine, or THC levels. The visual indicators 310 may emit or reflect light proportional to the amount of nicotine or THC consumed over the past 24 hours, the amount of nicotine or THC consumed during the current session, the estimated current plasma levels of a user, or the estimated average plasma levels of a user over the last 24 hours. The visual indicator 320 may indicate that a target minimum amount of nicotine or THC (for example, 0 mg) has been consumed over the last 24 hours. The visual indicator 330 may indicate that a predetermined maximum amount of nicotine or THC (for example, 30 mg) has been consumed over the last 24 hours.

[0057] FIG. 4 illustrates an alternative nicotine/THC delivery device 400 according to another exemplary embodiment of the present invention. The device 400 may be configured to deliver the nicotine/THC solution 112 similar to the device 100a or inhalation unit 110b-c. The device 400 may also include visual indicators 410₁-410_n that mimic the nicotine or THC consumption (or user nicotine, cotinine, or THC levels) of a traditional cigarette. Similar to the visual indicators 310, 320, and 330, the visual indicators 410₁-410_n may be any suitable device configured to selectively emit or reflect light. In the exemplary embodiment illustrated in FIG. 4, the visual indicators 410₁-410_n emit or reflect light in succession as nicotine or THC is consumed. As shown, visual indicator 420 emits or reflects light while the other visual indicators 410₁-410_n are off.

[0058] The visual indicators 410₁-410_n may be configured to output nicotine or THC consumption information proportional to the nicotine or THC included in a traditional cigarette. For example, visual indicator 410₁ may output a visual indication at the start of a smoking session. Visual indicators 410₂-410_n may emit or reflect light in succession as the user continues to use the device 400. The visual indicator 410_n may emit or reflect light when the inhalation sensor 200 estimates that the amount of nicotine or THC consumed by the user is equivalent to the amount of nicotine or THC in a tradition cigarette.

[0059] Alternatively, the output of the visual indicators 410₁-410_n may be proportional to another pre-determined maximum nicotine or THC consumption or user nicotine, cotinine, or THC level. The user nicotine, cotinine, or THC levels may be based on an estimated current level and an estimated average level over a specified time period. The device 400 may audibly (e.g., via an optional speaker) or visually (e.g., via the visual indicators 410₁-410_n) alert the user that the nicotine or THC consumption level has reached or exceeded a predetermined maximum consumption level. Additionally or alternatively, the device 400 may audibly or visually alert the user that the nicotine or THC consumption level has fallen beneath a target threshold to notify the user when the user may resume using the device 400.

[0060] In one exemplary embodiment, the visual indicators 310, 320, 330, 410, and/or 420 may be light emitting diodes (LEDs) or any other suitable device configured to emit light. In this instance, the visual indicators 310, 320, 330, 410, and/or 420 may receive power from the power supply 120a of the device 100 or the power supply of the inhalation unit 110b.

[0061] In another exemplary embodiment, the visual indicators 310, 320, 330, 410, and/or 420 may be an electronic paper display (e.g., an electrophoretic display, an electro-wetting display, an electrofluidic display, an interferometric modulator, a micro-electro-mechanical system, etc.)

or any other suitable device configured to reflect light. In this instance, the visual indicators 310, 320, 330, 410, and/or 420 may receive power from the power supply 120a of the device 100 or the power supply of the inhalation unit 110b. Alternatively, the power required to adjust the pixels of the electronic paper display may be supplied by an external device such as the charging unit 180.

[0062] In one exemplary embodiment, the visual indicators 310, 320, 330, 410, and/or 420 may be thermochromic, electrochromic, or electroluminescent polymers or paints. The polymers or paints may additionally have a color (or visibility) reversibility delay calibrated to an average of biological half-life of nicotine or THC, thus enabling the visual indicators 310, 320, 330, 410, or 420 to revert to the original color or visibility in a manner indicative of (*e.g.*, proportional to) the nicotine, cotinine, or THC level of the user. Alternatively, micro-scale capacitors wired in series (with or without a timer) with resistors may be utilized. In this instance, information indicative of nicotine or THC consumption (or nicotine, cotinine, or THC levels) may be output by applying power to a series of emitters (*e.g.*, LEDs) and/or activating electrochromic or electroluminescent polymers or paints and allowing the slow drain of the capacitors to restore the visual indicators to their original state in a manner indicative (*e.g.*, proportional) of the in a manner indicative of (*e.g.*, proportional to) the nicotine, cotinine, or THC level of the user.

[0063] In another exemplary embodiment, the visual indicators 310, 320, 330, 410, and/or 420 may be mechanical. The inhalation unit 110c of FIG. 1C, for example, may include an internal screw-based usage indicator mechanism. When the inhalation unit 110c mates with the charging unit 180b, the charging unit may rotate the screw-based usage indicator mechanism such that the visibility of colored tiles are adjusted.

[0064] The inhalation sensor 200 may limit the amount of nicotine or THC consumed over time. In instances where the device 100a-b includes a heating element 140, for example, the inhalation sensor 200 may prevent the heating element 140 from heating if the user has reached or exceeded a predetermined maximum nicotine/THC consumption level in a given time period (for example, a usage session, a daily limit, or any other measure of time) or a predetermined maximum user nicotine, cotinine, or THC level. Alternatively, the heating element 140 may be configured to output a reduced amount of heat if the user has reached or exceeded the predetermined maximum nicotine or THC consumption level in the given time period or the predetermined maximum user nicotine, cotinine, or THC level. In instances where the inhalation unit 110c does not include a heating element 140, the inhalation sensor 200 may prevent the reservoir 170 from refilling the inhalation unit 110c if the user has reached or exceeded the predetermined maximum nicotine or THC consumption level in the given time period or the predetermined maximum user nicotine, cotinine, or THC level. The predetermined maximum nicotine or THC consumption level or the user nicotine, cotinine, or THC level may be user adjustable.

[0065] FIG. 5 illustrates an alternative nicotine/THC delivery device 500 according to another exemplary embodiment of the present invention. The device 500 may be configured to deliver the nicotine or THC solution 112 similar to the device 100a or inhalation unit 110b-c. The device 500 may also include one or more user input devices 510 and 520 configured to adjust the predetermined maximum nicotine or THC consumption or user nicotine, cotinine, or THC level. The user input devices 510 and 520 may be, for example, dials or switches connected to a variable resistor. The inhalation sensor 200 may adjust the predetermined maximum nicotine or THC consumption or user nicotine, cotinine, or THC level based on the location of the user input devices 510 and 520.

[0066] In the exemplary embodiment illustrated in FIG. 5, the user input device 510 may be used to adjust the predetermined maximum nicotine/THC consumption for one session while the user input device 520 may be used to adjust a the predetermined maximum nicotine/THC consumption for one rolling 24 hour period. The user input devices 510 and 520 and inhalation sensor 200 may be calibrated such that user input devices 510 and 520 are aligned with visual indicators such as hash marks 512 and 522. The number of user input devices and the degree of freedom available for each user input device may be constrained by the size of the device 500.

Alternatively, the predetermined maximum nicotine/THC consumption or user nicotine/cotinine/THC levels may be preprogrammed or adjustable by a user through an external device in communication with the device 500 wireless or wired connection as described above.

[0067] Alternatively, the device 500 may include user input devices similar to user input devices 510 and 520 that allow a user to input one or more user biometrics. For example, the device may include a user input device that allows a user to input the user's weight.

[0068] The alternative nicotine/THC delivery device may include one or more alternate reservoirs that may include a reduced concentration of nicotine/THC solution 112 (either in addition to the reservoir 110 or in a separate portion of the reservoir 110). The alternate reservoir may enable a user to manually switch to a reduced concentration of nicotine/THC solution. Alternatively, the alternative nicotine/THC delivery device may automatically vaporize the reduced concentration nicotine/THC solution 112 in response to a determination by the inhalation sensor 200 that the user has consumed a predetermined maximum nicotine or THC amount or the user nicotine/cotinine/THC levels has reached a predetermined maximum level.

[0069] FIG. 6 illustrates an alternative nicotine/THC delivery device 600 according to another exemplary embodiment of the present invention. The device 600 may be configured to deliver a

nicotine/THC solution 112 similar to the device 100a or inhalation unit 110b-c. The device 600 may also include reservoirs 610, 612, and 614, for containing solution with three distinct concentrations of nicotine or THC.

[0070] For example, the reservoir 610 may include the highest concentration of nicotine or THC, reservoir 612 may include a reduced-concentration solution, and the reservoir 614 (on the back side of the device 600 relative to the viewer) may include a solution with no nicotine or THC. The device 600 may be configured to vaporize the solution in reservoir 612 until the user has reached or exceeded the predetermined nicotine or THC consumption target in a given time period, and then vaporize the reduced-concentrated solution (for example, by an alternate heating element and/or a reservoir injection system) in reservoir 614 until nicotine or THC consumption levels are reduced below the target level (or another pre-defined level of nicotine or THC consumption). The device 600 may also be configured to vaporize the solution in reservoir 614 if the user has reached or exceeded a second predetermined nicotine/THC consumption target in a given time period.

[0071] Alternatively, the device 600 may include an on-demand solution mixing device for electromechanically mixing pure nicotine or THC and solvents in a reservoir or directly into the heating element in order to provide a reduced-concentration solution 112.

[0072] FIG. 7 illustrates another view of the charging unit 180a illustrated in FIG. 1B and/or the charging unit 180b illustrated in FIG. 1C. As illustrated in FIG. 7, the charging unit 180 may include an input/output device 710, a visual indicator 720, and/or a visual indicator 730.

[0073] The input/output device 710 may any suitable device configured to receive input from a user and/or display information to a user. The input/output device 710 may be configured to enable a user to input or adjust the predetermined maximum nicotine/THC consumption level,

the predetermined maximum user nicotine/cotinine/THC level, static or dynamic biometric information, etc. The input/output device 710 may also be configured to output (*e.g.*, via a display) the predetermined maximum nicotine/THC consumption level, the maximum user nicotine/cotinine/THC level, static or dynamic biometric information, etc.

[0074] The visual indicator 720 or 730 may output information indicative of the user nicotine/THC consumption or user nicotine/cotinine/THC levels. Similar to the visual indicators 310, 320, 330, and 410, the visual indicator 720 or 730 may be any suitable device configured to selectively emit or reflect light.

[0075] In each of the exemplary embodiments described above, the inhalation sensor 200 may be used as a smoking cessation device. In some instances, the simple act of informing the user regarding nicotine or THC consumption or user nicotine, cotinine, or THC levels may reduce nicotine or THC consumption. In other instances, the user may be restricted from exceeding a predetermined maximum nicotine or THC consumption or user nicotine, cotinine, or THC level.

[0076] The inhalation sensor 200 may be configured to reduce the predetermined maximum nicotine/THC consumption or user nicotine/cotinine/THC level over a large time window (for example, days, weeks, months, etc.). The inhalation sensor 200 may be configured to account for human models of withdrawal. For instance, the inhalation sensor 200 may allow for high impulses upon wake and then further tapering throughout wakeful hours. Alternatively, the inhalation sensor 200 may be configured to mimic traditional cigarette profiles. For example, a user may prefer a nicotine consumption limit equivalent to one pack of traditional cigarettes per day, spaced out into 20 equal doses equivalent to one traditional cigarette each.

[0077] While exemplary embodiments have been set forth above, those skilled in the art who have reviewed the present disclosure will readily appreciate that other embodiments can be

realized within the scope of the invention. For example, while this disclosure describes regulating five distinct measures of nicotine or THC consumption with respect to time (peak nicotine/THC plasma levels, average nicotine/THC plasma levels, cumulative nicotine/THC consumption over a sliding window, cotinine levels over a sliding window, and nicotine/THC consumption per session) it is to be understood that other metrics are simply reconfiguration of the same logic (programmable variants) and should be encompassed by this application. Therefore, the present invention should be construed as limited only by the appended claims.

WHAT IS CLAIMED IS:

1. An inhalation sensor for an alternative nicotine or THC delivery device including a diluted nicotine or THC solution, the inhalation sensor comprising:
a processor; and
memory comprising:
a solution profile including information indicative of the nicotine or THC concentration of the diluted nicotine or THC solution; and
a device profile including information indicative of the nicotine or THC delivery device,
wherein the inhalation sensor is configured to determine an amount of nicotine or THC consumed by a user of the alternative nicotine or THC delivery device based on the solution profile and the device profile.
2. The inhalation sensor of claim 1, further comprising a timer and an inhalation timing sensor configured to detect an inhalation by a user,
wherein the inhalation sensor is configured to determine the amount of nicotine or THC consumed by the user further based on a duration of the inhalation.
3. The inhalation sensor of claim 2, wherein the inhalation sensor is configured to determine the amount of nicotine or THC consumed by the user further based on information indicative of a temperature of a heating element configured to vaporize the diluted nicotine or THC solution.

4. The inhalation sensor of claim 3, wherein the inhalation sensor is configured to determine the information indicative of the temperature of the heating element based on the duration of the inhalation.

5. The inhalation sensor of claim 4, wherein the device profile includes information indicative of a relationship between the duration of the inhalation and the temperature of the heating element.

6. The inhalation sensor of claim 3, wherein the inhalation sensor is configured to determine the amount of nicotine or THC consumed by the user further based on a time between the inhalation and a previous inhalation.

7. The inhalation sensor of claim 6, wherein the device profile further includes a ramp up profile indicative of the temperature of the heating element during inhalation and a decaying profile indicative of the temperature of the heating element after the heating element is de-activated.

8. The inhalation sensor of claim 3, wherein the solution profile further includes a burning point of the nicotine or THC solution.

9. The inhalation sensor of claim 8, wherein the inhalation sensor is further configured to determine a temperature of the heating element and compare the temperature of the heating element to the boiling point of the nicotine or THC solution.

10. The inhalation sensor of claim 9, wherein the inhalation sensor is configured to output an indication to the user in response to the temperature of the heating element approaching or exceeding the boiling point of the nicotine or THC solution.

11. The inhalation sensor of claim 9, wherein the inhalation sensor is configured to output a signal to the alternative nicotine or THC delivery device to interrupt the supply of power to the heating element in response to a determination that the temperature of the heating element approaching or exceeding the boiling point of the nicotine or THC solution.

12. The inhalation sensor of claim 1, further comprising:
a visual indicator configured to output a visual indication indicative of the amount of nicotine or THC consumed by the user.

13. The inhalation sensor of claim 12, wherein the visual indication is indicative of a comparison of the amount of nicotine or THC consumed by the user and an amount of nicotine or THC in a traditional cigarette.

14. The inhalation sensor of claim 1, wherein the inhalation sensor is configured to compare the amount of nicotine or THC consumed by the user to a nicotine or THC consumption limit.

15. The inhalation sensor of claim 14, wherein the nicotine or THC consumption limit is user adjustable.

16. The inhalation sensor of claim 15, wherein the inhalation sensor is configured to reduce the nicotine or THC consumption limit over time.

17. The inhalation sensor of claim 14, wherein the inhalation sensor is configured to output a signal to the alternative nicotine or THC delivery device to prevent further delivery of the diluted nicotine or THC solution in response to a determination that the amount of nicotine or THC consumed is greater than or equal to the nicotine or THC consumption limit.

18. The inhalation sensor of claim 14, wherein the inhalation sensor is configured to output a signal to the alternative nicotine or THC delivery device to interrupt a supply of power to a heating element in response to a determination that the amount of nicotine or THC consumed is greater than or equal to the nicotine or THC consumption limit.

19. The inhalation sensor of claim 14, wherein the inhalation sensor is configured to output a signal to the alternative nicotine or THC delivery device to interrupt a flow of the diluted nicotine or THC solution in response to a determination that the amount of nicotine or THC consumed is greater than or equal to the nicotine or THC consumption limit.

20. The inhalation sensor of claim 1, wherein the inhalation sensor is configured to determine the amount of nicotine or THC consumed by the user further based on biometrics of the user.

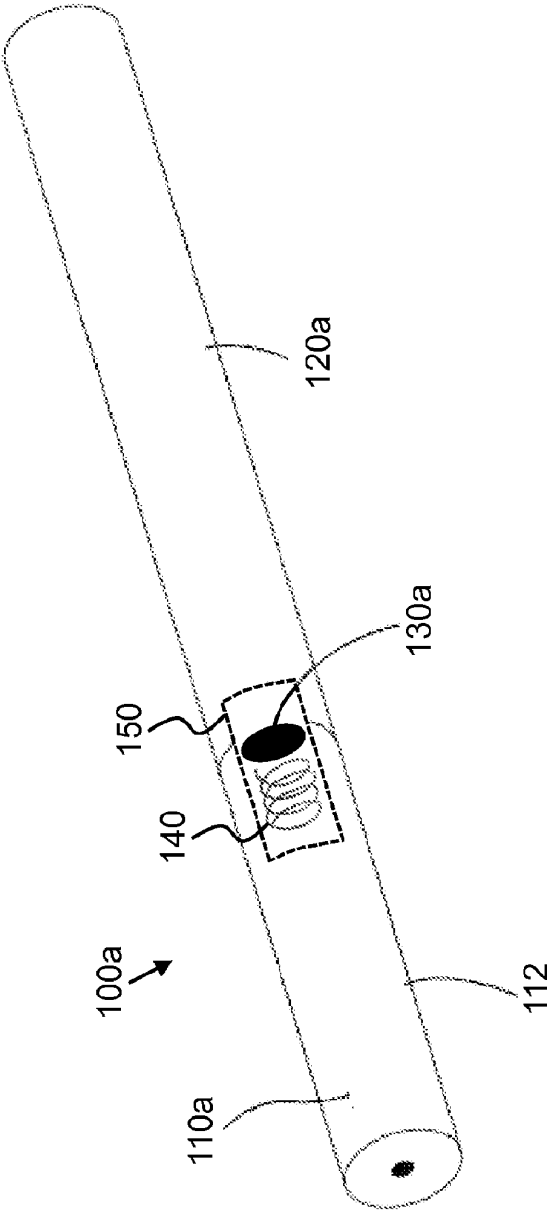
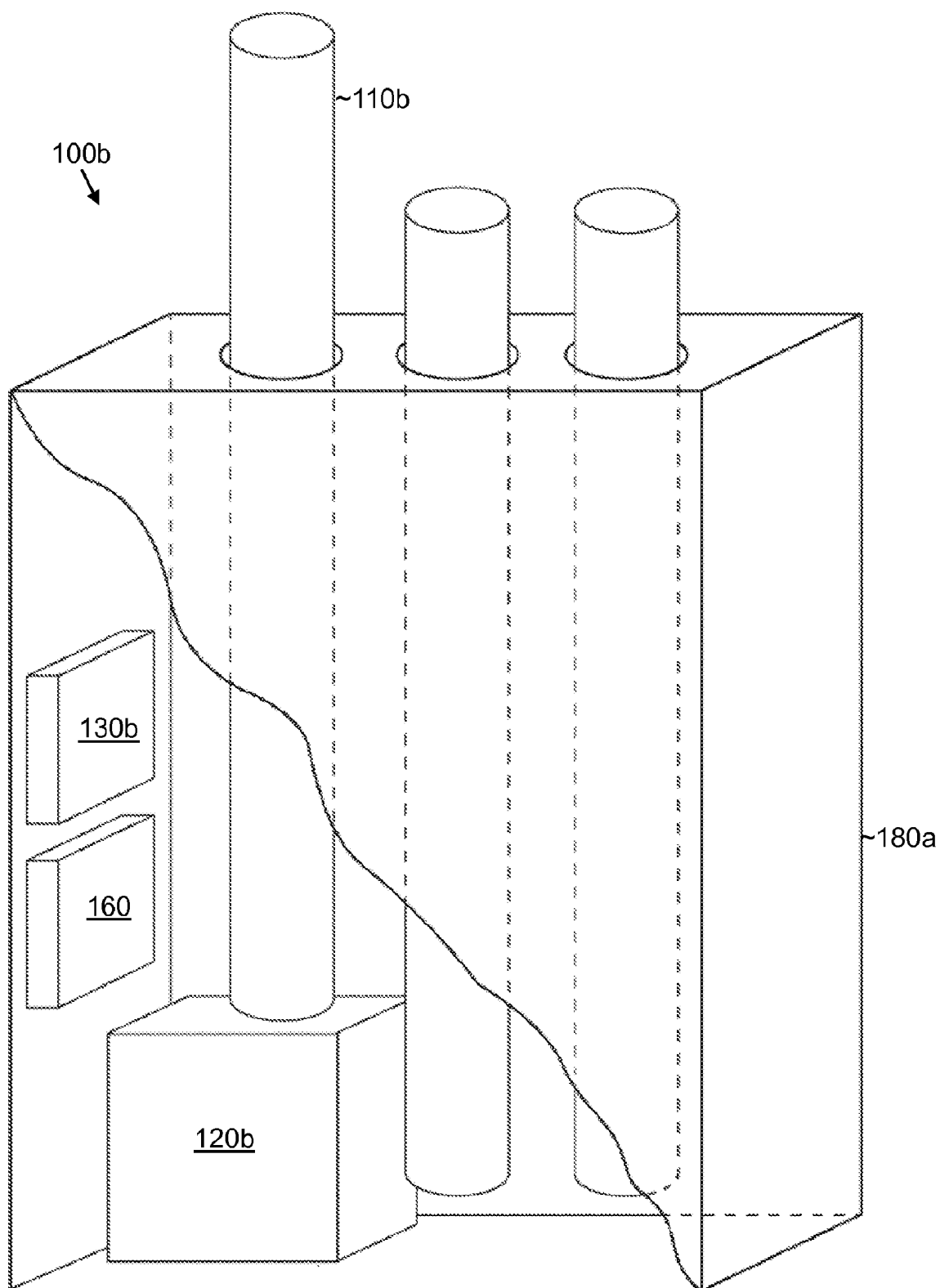
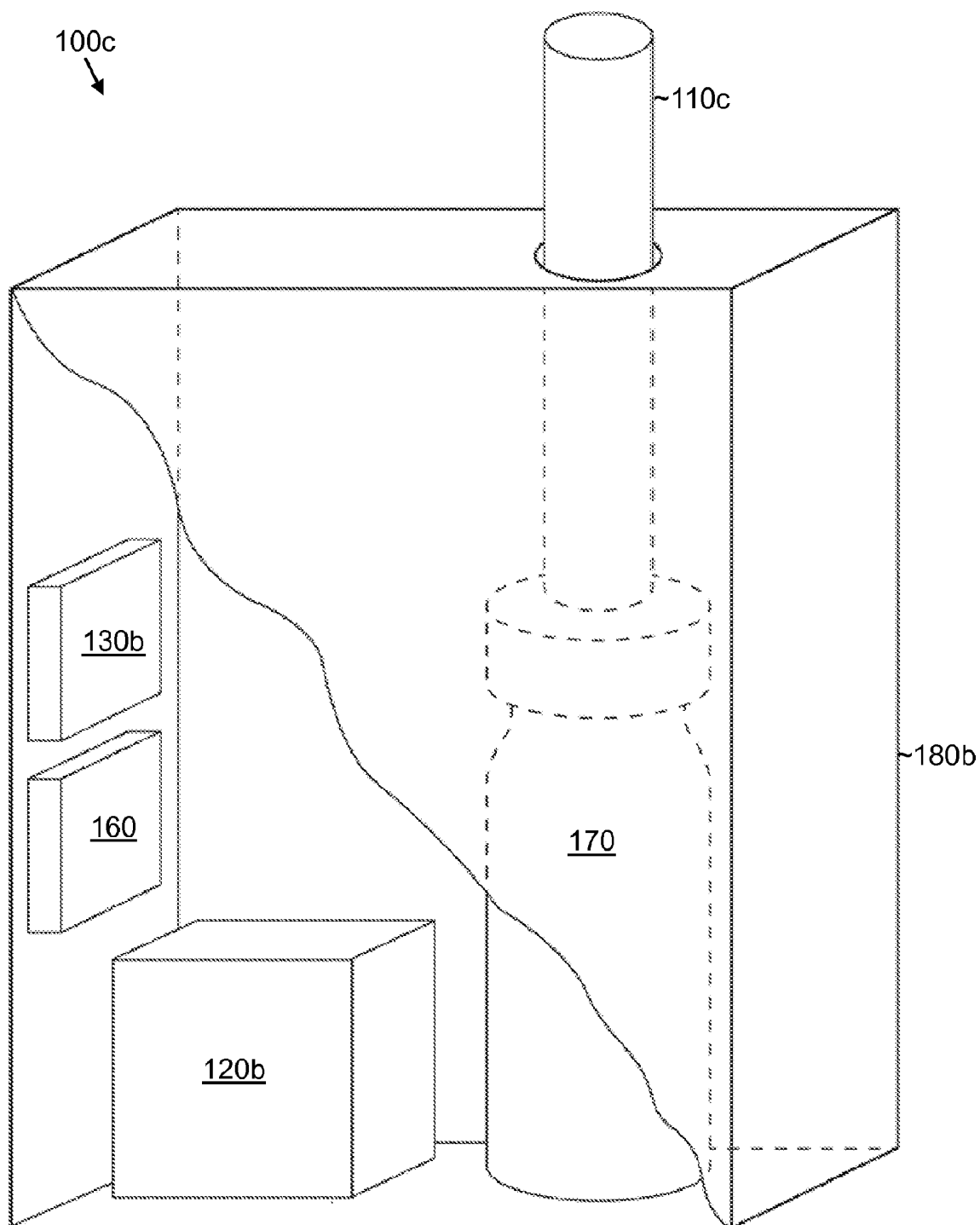


FIG. 1A

**FIG. 1B**

SUBSTITUTE SHEET (RULE 26)

**FIG. 1C**

SUBSTITUTE SHEET (RULE 26)

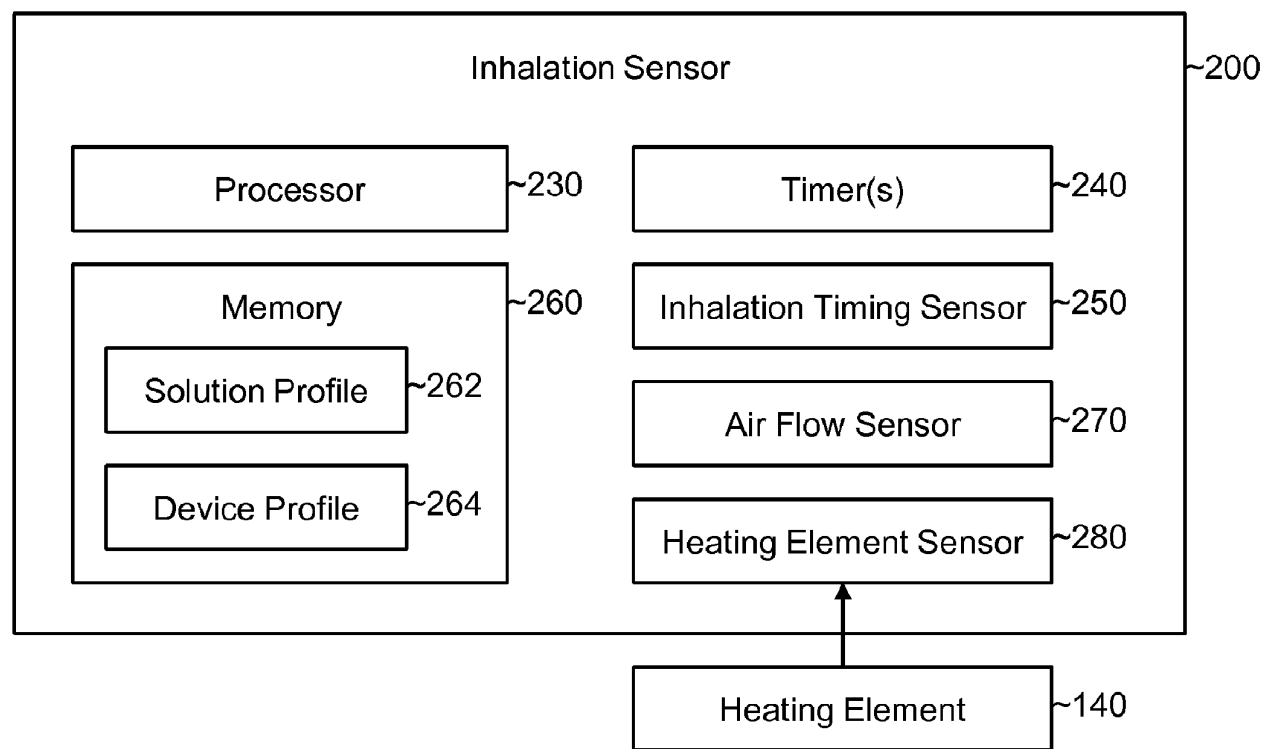


FIG. 2

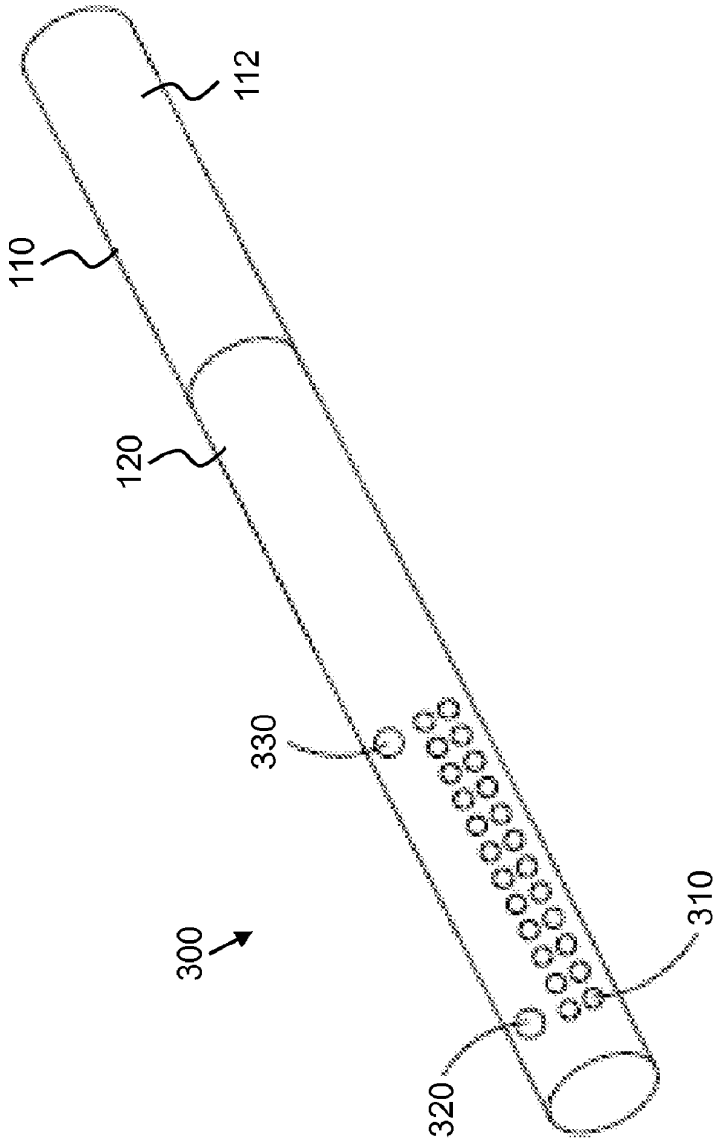


FIG. 3

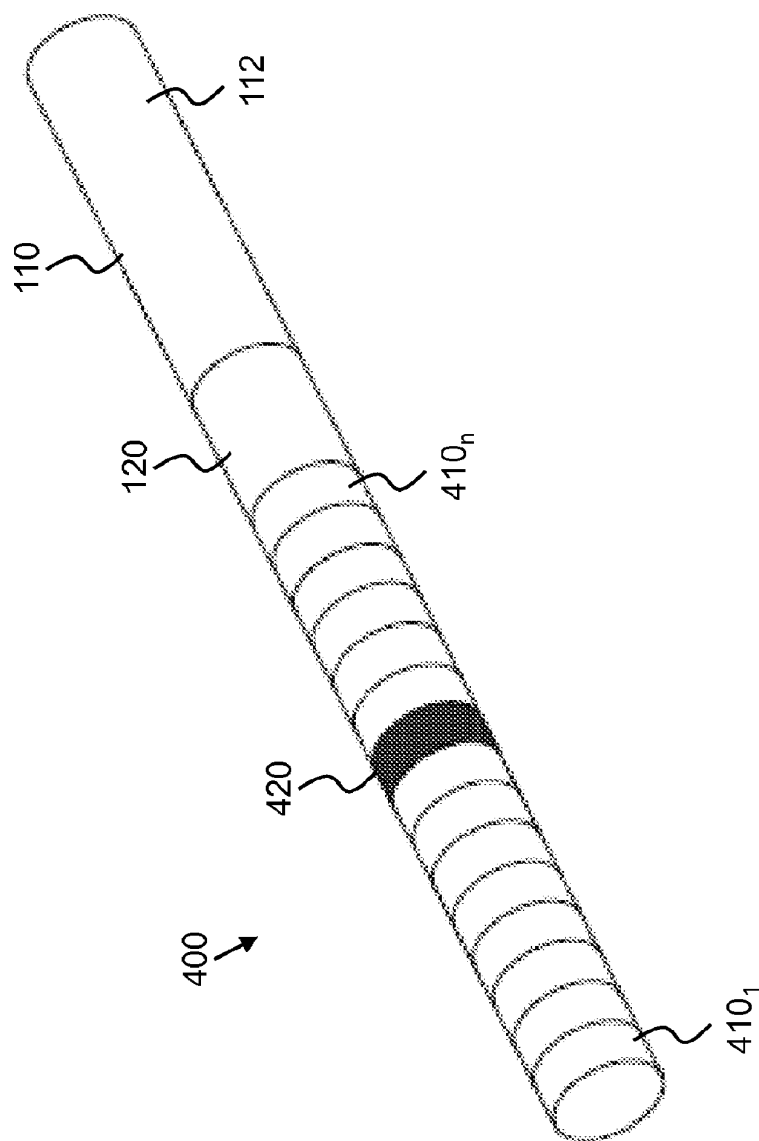


FIG. 4

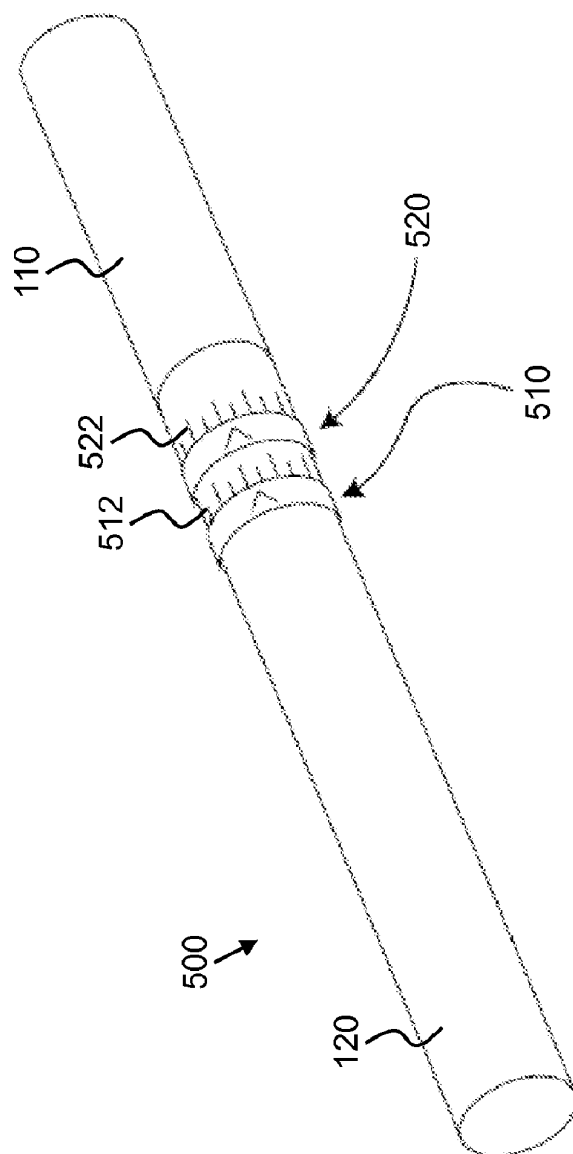


FIG. 5

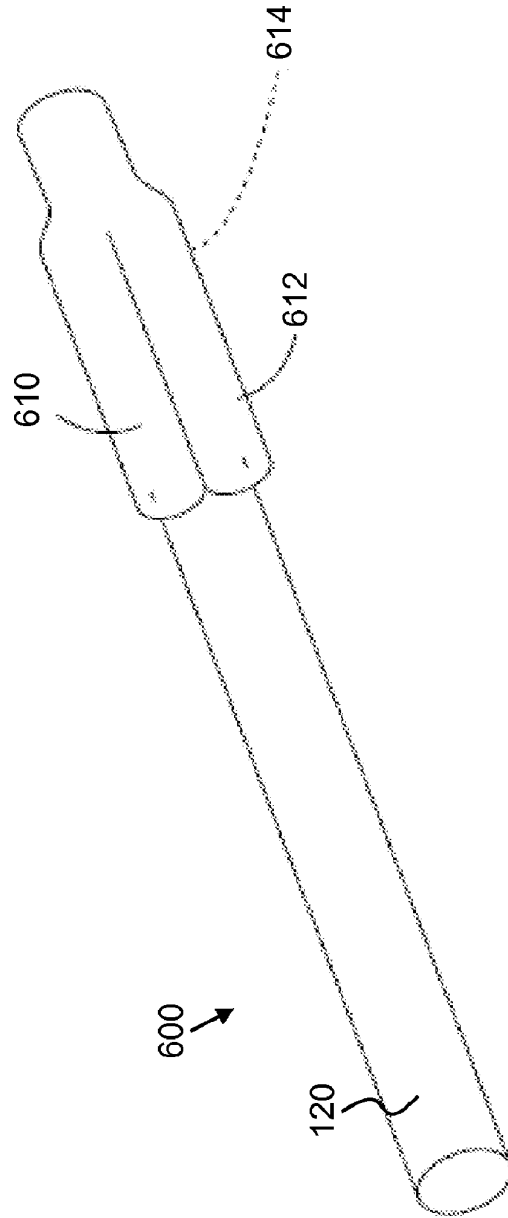
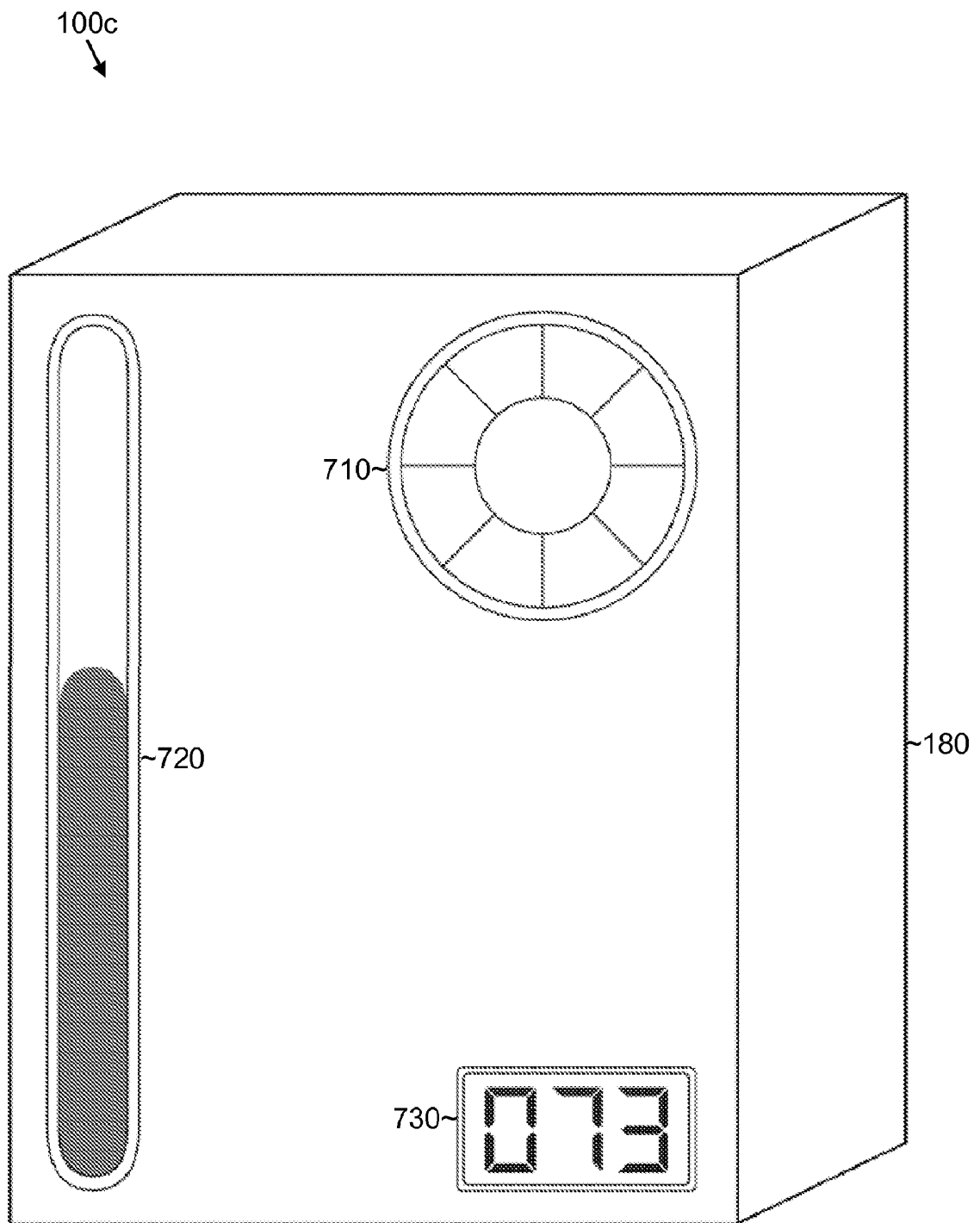


FIG. 6

**FIG. 7**

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 15/22299

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A24F 1/10 (2015.01)

CPC - A24C 5/3406

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A24F 1/10 (2015.01); CPC: A24C 5/3406

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 131/329, 131/330
IPC(8): A24F 1/10 (2015.01); CPC: A24C5/3406, A24F1/00, A24F47/00, A24F13/00, A24F47/008

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase, ProQuest Dialog, Google Web, Google Patents (Search terms: ecigarette, electronic cigarette, inhaler, vaporizer, nicotine, THC, dilution, solution, burning point, flash, boiling point, measure, consumed, temperature, ramp up, decay, indicate, LED, diode, limit, exceed, approach, profile, compare, conventional, traditional, report, etc.)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2012/0291791 A1 (Pradeep) 22 November 2012 (22.11.2012), para. [0014], [0019]-[0027], [0029], and [0047]-[0048], and Figs. 2 and 6.	1-6, 14-20 ----- 7-13
Y	US 4,947,875 A (Brooks et al.) 14 August 1990 (14.08.1990), col. 5, ln. 40-44, col. 6, ln. 36-45, col. 8, ln. 32-36, and ln. 64 to col. 9, ln. 4, col. 9, ln. 21-28, and col. 12, ln. 10-13.	7-11
Y	US 2008/0257367 A1 (Paterno et al.) 23 October 2008 (23.10.2008), para. [0010]-[0012] and [0016].	12-13
Y	US 8,667,891 B2 (Garcia et al.) 11 March 2014 (11.03.2014), col. 8, ln. 35-41, and col. 9, ln. 6-8, 10-12, and 22-33.	9-11

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

10 June 2015 (10.06.2015)

Date of mailing of the international search report

09 JUL 2015

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)



(51) International Patent Classification:
A24F 23/02 (2006.01)

(21) International Application Number:
PCT/US2015/031152

(22) International Filing Date:
15 May 2015 (15.05.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/994,787 16 May 2014 (16.05.2014) US

(71) Applicant: PAX LABS, INC. [US/US]; 660 Alabama
Street, 2nd Floor, San Francisco, CA 94110 (US).

(72) Inventors: BOWEN, Adam; 660 Alabama Street, 2nd
Floor, 2nd Floor, San Francisco, CA 94110 (US). MON-
SEES, James; 660 Alabama Street, 2nd Floor, 2nd Floor,
San Francisco, CA 94110 (US).

(74) Agent: WHEELER, Matthew; Wilson Sonsini Goodrich
& Rosati, 650 Page Mill Road, Palo Alto, CA 94304 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG,
MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM,
PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC,

[Continued on next page]

(54) Title: SYSTEMS AND METHODS FOR AEROSOLIZING A SMOKEABLE MATERIAL

(57) Abstract: A smoking device for generating and releasing smoking vapor free from con-
tamination into the mouth of a user comprising a mouthpiece for providing vapor for inhala-
tion to a user including a tubular casing containing a heater for heating a smoking substance
at a substantially constant low temperature by regulating the flow of fuel by a thermal regu-
lator and further having means for visual indication of the operation of the device.

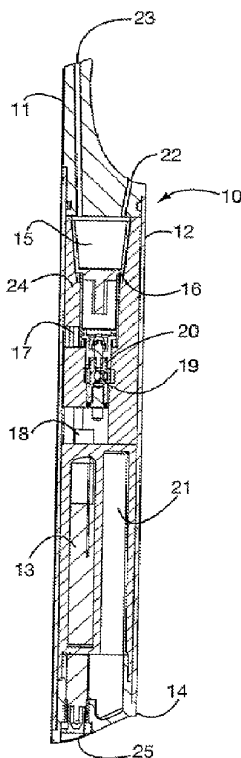


FIG. 2



SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

- *with international search report (Art. 21(3))*

SYSTEMS AND METHODS FOR AEROSOLIZING A SMOKEABLE MATERIAL**CROSS-REFERENCE**

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial No. 61,994,787 filed May 16, 2014, which is entirely incorporated herein by reference.

BACKGROUND

[0002] Smoking devices, such as cigarette holders and pipes are well known in the art for providing flavored vapor from a smokeable substance to a user for therapeutic and smoking pleasure. However, existing devices used have no control of heating and combustion of the tobacco products. The devices tend to produce toxic, tarry and carcinogenic by-products which are harmful and also impart a bitter and burnt taste to a mouth of a user.

[0003] A further problem is that there is no control of contamination of the inhaled vapor mixture with heater exhaust gases, due to inappropriate proportioning and location of the inlets and the exhaust vents. Typically, the exhaust gas is used to directly heat the tobacco, and those gases contain harmful byproducts of incomplete combustion.

[0004] In an effort to overcome these deficiencies, there is a need for providing a device structure and substance for producing vapor for smoking which is free from harmful by-product and provides a cool and soothing vapor for smoking.

SUMMARY

[0005] The present invention is directed to improvements in smoking devices, particularly to smoking articles which employ a formed smokeable material cartridge as a source of producing vapor by heat transfer to the cartridge by conduction, convection and/or radiation for smoke and flavor. The present invention relates to self-contained vaporization devices, and more particularly, to a low-temperature vaporization device for use with tobacco, botanicals or other smokeable products. The device is of an elongated main body with a mouthpiece at one end and an attached tubular casing at the other end having a vaporization chamber and a heater. The mouthpiece and the casing form a unitary unit. The device can be portable.

[0006] The present invention is drawn to a novel smoking device consisting of a mouthpiece and a casing having a heater, a low temperature vaporization chamber, a fuel tank, an igniter with control means for maintaining equilibrium point by keeping the operating temperature below about 400 F. In some examples, the operating temperature is below 350 about F. In order to maintain a stable operating temperature, a thermal regulator can be used to control flow rate of the fuel.

[0007] Further provided herein is a mouthpiece made of a high temperature food-safe material, such as ceramic, glass, or high temperature plastics known as PEI resin (brand name Ultem). However, suitable plastic or wood, etc., can also be used but may additionally require an insulating material to prevent excessive heat reaching the user's lips.

[0008] Additionally, air inlets are directed downwards, so that fresh ambient air drawn through mixes with the vapor generated into the vaporization chamber located above the smokeable substance cartridge, which is extracted from the cartridge by inlets located below the cartridge and drawn into user's mouth for inhalation.

[0009] It is another object of the invention to provide air inlet or inlets having a diameter and direction sized to admit ambient air into the chamber to heat up the substance and not effect the operating temperature and also regulating the velocity of ambient air entering and mixing with the vapor generated heating in the chamber at such a rate that the proportionate inhalation passage provides a perception to the user as if the smoke is drawn through a cigarette.

[0010] It is still another object of the invention to provide a heater which is separated from the vapor chamber by an insulating medium such as ring made of PTFE, ceramic or other insulating material and thereby preventing the exhaust gases produced by the heater from entering and contaminating the vapor in the vaporization chamber collected for inhalation.

[0011] Another object of the invention provides a heater formed of a conductive shell and a catalyst. The shell may be of one or more material formed by welding or pressing together. The catalyst can be of platinum or palladium impregnated metal or glass or other suitable material, which provides for efficient flameless combustion of the fuel and glows red when heated to indicate that the device is activated. Additionally, a feedback loop can be employed to regulate the desired temperature.

[0012] In some implementations, the smokeable material cartridge may be formed and shaped for easier insertion into the heating chamber and to snugly fit into the cavity of the heating chamber for improved thermal conduction and vaporization. The cartridges may be formed and wrapped into a wrapper. In some implementations, the smokeable material may be provided in a loose form in a pouch. The wrappers and pouches may be formed of a material which does not produce significant amount of harmful gases.

[0013] An aspect of the present disclosure relates to a cartridge fitted in a device, the cartridge comprising a permeable pouch containing a smokeable material, wherein the device is configured to heat the smokeable material in the permeable pouch, and wherein the permeable pouch allows an exit of a vapor generated from the heating of the smokeable material.

[0014] Additional aspects and advantages of the present disclosure will become readily apparent to those skilled in this art from the following detailed description, wherein only illustrative embodiments of the present disclosure are shown and described. As will be realized, the present disclosure is capable of other and different embodiments, and its several details are capable of modifications in various obvious respects, all without departing from the disclosure. Accordingly, the drawings and description are to be regarded as illustrative in nature, and not as restrictive.

INCORPORATION BY REFERENCE

[0015] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF DRAWINGS

[0016] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings or figures (also “FIG.” and “FIGs.” herein), of which:

[0017] FIG. 1 is a side view of a vaporization device.

[0018] FIG. 2 is a sectional view of the vaporization device in FIG. 1.

[0019] FIG. 3 is a perspective view of a heater.

[0020] FIG. 4 is a cutaway view of an alternate vaporization device.

[0021] FIG. 5 is a sectional detail view of a cartridge.

[0022] FIG. 6 is a perspective view of a cartridge.

[0023] FIG. 7 is a sectional detail view of a cartridge.

[0024] FIG. 8 is a sectional detail view of a cartridge.

[0025] FIG. 9 is an example of a pouch in a vaporization device.

[0026] FIG. 10 is an example of an oven chamber of a device.

DETAILED DESCRIPTION

[0027] Referring to FIG. 1 and FIG. 2, the exterior of the device 10 comprises a mouthpiece 11, a tubular case 12, and the base 14 of a butane tank 21. The mouthpiece is removable and creates an airtight seal with the interior of the case. With the mouthpiece removed, a cartridge (FIG. 5) is introduced to vaporization chamber 15 of a heater 16. The mouthpiece is then reinserted to close the device.

[0028] The mouthpiece is made of a high-temperature and food-safe material such as ceramic, glass, or various high-temperature plastics such as PEI resin (brand name Ultem). Design is simplified by use of high temperature materials, but standard plastics or wood, etc, can also be used with the addition of an insulating component that prevents any excessive heat from reaching the user's lips.

[0029] To activate the device, the butane tank is pulled axially outward, partially removing it from the case. This starts the flow of butane by opening a master valve 18, and then activating a piezoelectric igniter 13. The tank remains in the partially removed position for the duration of use. While the master valve is open, butane flows through a thermal regulator 17, and into the carburetor 20. Ambient air enters the case through slot 19. A venturi in the carburetor entrains air, causing it to mix with the butane. The mixture then flows into the heater 16.

[0030] The lead of the ignitor is positioned in the heater. With the spark of the ignitor (immediately following the start of gas flow) the gas ignites and heat starts conducting throughout the heater. Heat transfers to the cartridge by conduction, convection and/or radiation. The cartridge is shaped to fill the chamber, so as to maximize surface contact for thermal conduction.

[0031] As the cartridge heats, vapor generates within the cartridge and in the space immediately above it. When a user draws on the device, fresh air enters through air inlet 22, mixes with the vapor, and the mixture is delivered to the user via the inhalation passage 23. The air inlet or inlets can be directed downward, so as to improve the extraction of vapor from the cartridge. They can also be directed along a diagonal through the mouthpiece, or laterally through the case itself, above the cartridge.

[0032] FIG. 3 depicts a detailed view of the heater 16. The heater comprises a thermally conductive shell 26 and catalyst 27. The shell can be comprised of one material, or a combination of materials welded or pressed together. The catalyst can be platinum- or palladium-impregnated metal or glass, or other suitable material known to those skilled in the art. The catalyst provides for efficient flame-less combustion of the butane. The vent 28 of the heater is positioned such that it is visible through the slot 29 of the body as shown in FIG. 1. This allows the user to see the catalyst which, when heated, can glow red to indicate that the device has been activated.

[0033] Referring again to FIG. 3, adjacent to the heater and in intimate thermal contact is the thermal regulator 17. As the temperature of the heater increases, so does that of the regulator. The regulator is designed to restrict the flow of butane as the temperature increases, thus creating a feedback loop. The regulator can consist of a bimetallic strip 60 and silicone tubing 61 which is the conduit of the butane. The two are arranged such that as the bimetallic strip heats up, it curls

to pinch the silicone tube and thereby restrict the flow of butane. The reduced flow of butane results in less heat generated. The heater subsequently cools down, and so does the regulator, allowing more butane to flow again. The overall result is that a stable operating temperature is established in the heater. Such a system can be readily tuned to achieve an operating temperature that varies by less than +1-5 degrees Fahrenheit.

[0034] The regulator further comprises a moveable backplate 62 which allows adjustability of the operating temperature by adjusting the temperature at which the bimetallic actuator closes the tube valve. This is to be performed once at manufacture, to calibrate the device. Alternatively, a control means may be used to allow the target temperature of the device changed during operation.

[0035] The regulator can comprise in part a bimetallic strip and silicone tubing valve. Alternatively, the regulator can be comprised of other materials and configurations, as described later.

[0036] The desired operating temperature for vaporizing the smokeable materials herein can be below about 400 F. In some cases, the operating range can be below about 350 F. For example, for the purposes of vaporizing most botanicals in this device, the desired operating temperature is below about 400 F, or, in some cases, below about 350 F.

[0037] The air inlet diameter can be sized such that inhalation is somewhat inhibited. This allows time for ambient air entering the chamber to heat up and not affect operating temperature considerably. It also increases velocity of the entering air, which improves circulation and mixing in the vaporization chamber. It also creates a partial vacuum, lowering the vapor point temperature for material contained in the vaporization chamber. The reduction in draw rate can also serve to give the impression of drawing on a cigarette or pipe. Both the fresh air inlet and inhalation passage can be adjusted to provide appropriate draw rate for the operating temperature of the device, and the perception intended for the user.

[0038] Once the cartridge is consumed, the device is turned off by pushing the tank back into the case, closing the master valve. The spent cartridge is removed by opening the device and turning the body over. The cartridge can simply fall out. Alternatively, a mechanism can be used to quickly and easily remove the cartridge. This mechanism can include, but does not require, the use of a pin or slide part to eject the cartridge as another part of the device is moved or removed. The removal mechanism can also involve introduction of a foreign object.

[0039] In some implementations,, the mouthpiece may be permanently attached to the body. In that case, the vaporization chamber may be accessed by operating a sliding or hinged door, or similar means, built into the device.

[0040] The heater of the device is fitted into the case with an insulator 24. The insulator can be made of PEI (brand name Ultem), ceramic, or other insulating material. The insulator serves to minimize thermal transfer from the heater to the case, while creating an air-tight seal. The seal prevents exhaust gases produced by the heater from entering the vaporization chamber. Exhaust gases are instead vented out the case slots. Since the air inlet is distant from the slots, there is substantially no contamination of the inhaled vapor mixture by heater exhaust gases.

[0041] In some implementations, the insulator can be a partially hollow shell, containing a sealed vacuum. In yet other implementations, the heater may be sealed directly to the case by braising in a vacuum furnace, so as to create a vacuum between the two and obviate need for an insulator component.

[0042] The tank can be made of a translucent material. This allows the user to determine the level of fuel remaining by looking at the base of the tank.

[0043] The case can be made of a material that is either a good thermal conductor (such as aluminum), or a poor one (such as ceramics). In both cases, the effect is that the body remains cool enough to touch over a large portion of its surface.

[0044] In one example, a bimetallic actuator can be used in the regulator. In another example, a shape memory alloy actuator such as nickel-titanium alloys ("Nitinol") can be used. In yet another example, a paraffin-filled component that expands and contracts to modulate butane flow can be employed. In a further example, a system can be employed to measure the current temperature, e.g., with a thermocouple sensor and compare it to a prescribed temperature, e.g., with a micro-controller, and by controlling an electromechanical valve, e.g., servo or solenoid valve. In a configuration with user-selected temperature, as described above, the selected temperature can be used as an input to this system.

[0045] A thermal regulator may be used. Alternatively, the device may be constructed without an active regulating element. This may result in reduced complexity and in lowering the overall cost of the device. In this case, the flow of butane is set at a low level. In use, the temperature inside the chamber increases until an equilibrium point where additional heat introduced equals the heat lost to the environment. Heat is lost by conduction through the body of the device, and with the vapor delivered to the user. This equilibrium point determines the operating temperature of the device. By changing the butane flow rate, size and material of the burner, and other factors, the system can be calibrated to provide a fairly stable desired operating temperature.

[0046] An advantage of the bimetallic regulator feedback loop methods over the equilibrium method is that the operating temperature is not dependent on environmental factors such as ambient temperature and wind.

[0047] A piezo-electric ignitor can be used. Other ignitors may be used, such as, a flint starter or battery-powered resistive coil.

[0048] The butane tank may be refillable, and may have a port 25 for that purpose. Alternatively, the tank may be disposable once its fuel is exhausted. A release mechanism such as a pin or cam may be employed allowing the user to quickly remove the depleted tank and replace it with a full one. The replaceable tank may include additional parts of the device including, but not limited to, the ignitor and heater. Butane can be used as the fuel source, but may be replaced by other liquid fuels, such as ethanol.

[0049] Various means of feedback may be used to indicate the following states or metrics of the device: 1) the device is on, 2) the current temperature of the vaporization chamber, 3) the chamber is below a prescribed operating temperature, 4) the chamber has reached a prescribed operating temperature and vapor is ready for consumption, and 5) the chamber has exceeded a prescribed operating temperature.

[0050] The means of the feedback includes both physical and electronic implementations. Possibilities include thermochromatic paint, light-emitting diodes and liquid crystal display. The sensing and control means for electronic feedback can be implemented by use of thermocouple and micro-controller, as is known to those skilled in the art.

[0051] The smokeable materials herein may include, but are not limited to, tobacco, botanicals (e.g., cannabis, chamomile), pharmaceuticals, nutraceuticals, natural or artificial flavorants, coffee grounds or coffee beans, mint, lemon, honey, tea leaves, cocoa, or any other substance providing a benefit or sensation to an end user.

[0052] The smokeable materials herein may be provided in loose leaf form, cut form, shredded form, chopped form, packed form, or any other natural or processed form. As described elsewhere herein, in some examples, the smokeable material may comprise fine pieces of tobacco. In other examples, the smokeable material may comprise loose leaf tobacco. In yet other examples, the smokeable material may comprise loose leaf, shredded or chopped botanicals (e.g., loose leaves, shredded). The smokeable material comprise a vapor forming medium (e.g., glycerin).

[0053] Active elements contained in botanicals may vaporize at different temperatures. The device may be calibrated to establish a single stable temperature, intended for vaporizing solely tobacco or solely chamomile, for example. A control means may be used to select a variety of temperature settings. The user may choose which setting based on the type of cartridge used. The control means can effect a desired temperature mechanically, such as by changing flow rate of

the valve, or electronically, such as by electromechanical valve and micro-controller intermediary.

[0054] In some examples, butane may provide the most energy-dense and practical fuel source. In some examples, the butane heating system is replaced by a battery-powered electric heater or other compact heat source.

[0055] FIG. 4 depicts a cutaway view of a vaporization device which more closely resembles a traditional pipe form. In this configuration, the device retains all of the critical elements from the configuration in FIG. 1. The user inserts a cartridge 40, under a sliding top piece 41, where the cartridge mates with the heater 42. Fuel held in the tank 43 is released by turning dial 44 to open master valve 45. The fuel travels through the regulator 51, and then through the carburetor 46 where it draws in air through the intake port 47 and catalyzes in a manner similar to that of the configuration in FIG. 1. As the cartridge 40 reaches its operating temperature the user places the mouthpiece 48 in their mouth and draws air in through the inhalation intake port 49 and through the vapor passage 50 where it is pre-cooled.

[0056] A cartridge comprising the smokeable material may be fitted in the device 10. The device can be configured to heat the smokeable material in the cartridge. The device can heat the smokeable material (e.g., in the vaporization chamber) to a temperature required to vaporize the smokeable material. The cartridge can be inserted into the heated vaporization chamber of the device. For example, the device can heat the cartridge to below about 400 F. The cartridge may comprise a wrapper, a permeable pouch or a perforated container.

[0057] In some examples, the smokeable material (e.g., a moist smokeable material that may need to be contained in a wrapper) may be provided in a wrapper. The wrapper may be provided with a perforation that allows an exit of a vapor generated from heating the smokeable material. The perforation may further comprise an aeration well that allows air to access the smokeable material.

[0058] In some examples, the smokeable material (e.g., dry and/or loose smokeable material that may not need to be contained in a wrapper) may be provided in a permeable pouch. The pouch may be permeable to gases (e.g., air, vapor generated from heating the smokeable material, etc.). The permeable pouch may allow air to access the smokeable material. The permeable pouch may allow an exit of a vapor generated from heating the smokeable material. The permeable pouch may eliminate the need to directly expose the smokeable material to the surroundings (e.g., by leaving a portion of the smokeable material exposed, as shown, for example, in FIG. 7, or by providing perforations, in some cases together with aeration wells, that allow vapor to exit and/or air to enter, as shown, for example, in FIGs. 5, 6 and 8). The permeable pouch may eliminate the

need to puncture the cartridge. The permeable pouch may be permeable on all surfaces. All surfaces of the permeable pouch may be permeable. The permeable pouch may comprise one or more permeable surfaces. Further, the permeable pouch may enhance air and vapor transport to and from the smokeable material (e.g., by providing air and vapor transfer across a larger surface of the pouch as compared to the vapor transfer available in a cartridge that only has a single or more than one perforations on one or two sides).

[0059] In some examples, the smokeable material (e.g., dry and/or loose smokeable material that may not need to be contained in a wrapper) may be provided in a perforated container. The perforated container may comprise or be formed of a metallic foil (e.g. aluminum, stainless steel, or copper) with a perforation pattern to allow gas transfer through the container. The perforated container may have a perforation pattern on at least one surface of the container. The perforated container may allow air to access the smokeable material. The perforated container may allow an exit of a vapor generated from heating the smokeable material. The perforated container may eliminate the need to directly expose the smokeable material to the surroundings. The perforated container may eliminate the need to puncture the cartridge. Further, the perforated container may enhance air and vapor transport to and from the smokeable material (e.g., by providing air and vapor transfer across a larger surface). The perforated container may comprise or be formed of a thermally conductive material to enhance heat transfer to the smokeable material. The perforated container may be perforated on all surfaces. All surfaces of the perforated container may comprise perforations. The perforated container may comprise one or more perforated surfaces. Further, the perforated container may enhance air and vapor transport to and from the smokeable material (e.g., by providing air and vapor transfer across a larger surface of the container as compared to the vapor transfer available in a cartridge that only has a single or more than one perforations on one side or only on two opposing sides).

[0060] Any aspects of the disclosure described in relation a cartridge comprising a wrapper may equally apply to cartridges comprising a permeable pouch or a perforated container at least in some configurations. Any aspects of the disclosure described in relation a cartridge comprising a permeable pouch may equally apply to cartridges comprising a wrapper or a perforated container at least in some configurations. Any aspects of the disclosure described in relation a cartridge comprising a perforated container may equally apply to cartridges comprising or a wrapper or a permeable pouch at least in some configurations.

[0061] FIG. 5 depicts a sectional view of an example of a cartridge 30. The cartridge consists of a smokeable material 31, enclosed in a wrapper 32, with perforations 33, and aeration wells 34. The wrapped cartridge allows for the easy insertion and disposal of smokeable material (e.g.,

tobacco material, botanicals, or any other smokeable material herein) without creating a mess, while the perforations allow the formed vapor to be released. When the cartridge is used up it can be easily disposed of in its entirety.

[0062] Smokeable material, such as, for example, tobacco or tobacco material, may be any combination of natural and synthetic material that can be vaporized for pleasure or medicinal use. In an example, a test cartridge is prepared using flue-cured tobacco, glycerin, and flavorings. Those skilled in the art of tobacco product manufacture are familiar with these and other ingredients used for cigarettes, cigars, and the like. The cartridge is produced by chopping tobacco into fine pieces (less than 3 mm diameter, preferably less than 2 mm; having no dimension larger than 3 mm, or having substantially all fine pieces be less than 2 mm in all dimensions), adding the other ingredients, and mixing until even consistency is achieved.

[0063] The cartridge may be substantially cylindrical. In other implementations, the form can be modified for various reasons. As an example, the walls of the cartridge may be drafted for easier insertion into the vaporization chamber. Or, the bottom of the cartridge may possess receptacles, which when combined with complimentary features on the surface cavity of the vaporization chamber may allow for more surface contact and hence improved thermal conduction. The wrapper may be formed as a pouch in some implementations.

[0064] Any material may be used for the wrapper, provided that when heated to the operating temperature, it does not produce significant amounts of harmful gases. Aluminum foil and parchment paper are two examples. With papers, the cartridge may be manufactured in a folded-cup design, similar to that shown in FIG. 6. With films or metal foils, the wrapper can be pressed or blow-molded to the appropriate shape.

[0065] During manufacture, the cartridge may be enclosed on all sides, and perforated on the top so that vapors can emanate upwards. In the perforation step, or in an additional step, the optional aeration wells may be created.

[0066] The cartridge may be wrapped on all sides but leaving the top exposed, as shown in FIG. 7. This is possible since the purpose of the wrapper is primarily to prevent tobacco material from touching the sides and bottom of the vaporization chamber.

[0067] In another implementation, the material for the top of the cartridge may be vapor permeable, such that perforations are not necessary. As described in greater detail elsewhere herein, cartridges of the disclosure may also be air permeable. Such air and vapor permeable cartridges may advantageously be used to enhance air and vapor transfer along one, two or more (or all) surfaces of the cartridge.

[0068] In another implementation, the cartridge as purchased by the user has no openings, but is punctured prior to insertion into the device, or upon introduction to the vaporization device. The latter can be achieved by adding a hollow puncturing means to the mouthpiece part of the device. For example, the inhalation passage of the mouthpiece can be extended by a hollow tube. When the mouthpiece is reinserted to close the device, it pierces the cartridge previously introduced, and allows a path for vapor to exit to the user.

[0069] In some examples, the tobacco material may be a homogenous mixture. In other examples, there may be two layers, as shown in FIG. 8. The moist layer 35 has higher content of vapor-forming material than the dry layer 36, which consists of dry tobacco or other material acting as a filter. The dry layer serves to prevent any liquid from bubbling up and out of the cartridge during heating.

[0070] In some examples, a lower compartment may consist entirely of a vapor-forming medium, such as glycerin. An upper region may consist of the tobacco material to be vaporized, and the two may be separated by a material that only allows the medium to pass in a vapor or gaseous phase. Gore-tex (brand name) is one such material. In use, vapor generated in the lower region may pass through the semi-permeable membrane, volatilize the active components of the tobacco, and a mix of the two may be delivered to the user upon inhalation.

[0071] In some implementations, the consistency of the tobacco material is such that the wrapper is not necessary. This is possible if at least the outer surface of the cartridge is dry and cohesive enough to not leave deposits inside the device. Such a cartridge can be made by forming tobacco material in a mold. If the resulting surface is excessively moist, it can be dried by heating the cartridge in an oven.

[0072] The cartridge 30 may comprise a permeable pouch containing a smokeable material. The permeable pouch may comprise cellulose and/or other permeable materials (e.g., other fibers) capable of withstanding the operating temperatures of the device. The permeable pouch may comprise a binding agent or binder (e.g., cellulose acetate fibers). The binding agent or binder may be capable of withstanding the operating temperatures of the device (e.g., during heating of the smokeable material in the permeable pouch) without vaporizing ("off-gassing"). The binding agent may be safe for inhalation by a user. Thus, the permeable pouch may be capable of withstanding the operating temperatures of the device (e.g., during heating of the smokeable material in the permeable pouch) while remaining intact. The permeable pouch may be heat-sealed (e.g., at a temperature of about or exceeding the operating temperature of the device). The permeable pouch may be permeable to air, and/or vapor (e.g., vapor generated from heating the smokeable material). The permeable pouch may contain a given quantity of smokeable material.

The given quantity of smokeable material may be chosen based on device dimensions, duration of smoking time, or desired smoke or vapor composition.

[0073] The cartridge 30 may comprise a perforated container containing a smokeable material. The perforated container may comprise a metallic foil with a perforation pattern on at least one surface. The perforated container may be welded shut or the perforated container may comprise a binding agent or binder (e.g., cellulose acetate fibers). The binding agent or binder may be capable of withstanding the operating temperatures of the device (e.g., during heating of the smokeable material in the perforated container) without vaporizing (“off-gassing”). The binding agent may be safe for inhalation by a user. Thus, the perforated container may be capable of withstanding the operating temperatures of the device (e.g., during heating of the smokeable material in the perforated container) while remaining intact. The perforated container may be heat-sealed (e.g., at a temperature of about or exceeding the operating temperature of the device) or welded. The perforated container may allow passage to air, and/or vapor (e.g., vapor generated from heating the smokeable material). The perforated container may contain a given quantity of smokeable material. The given quantity of smokeable material may be chosen based on device dimensions, duration of smoking time, or desired smoke or vapor composition. The perforated container may be formed as a pouch in some implementations.

[0074] FIG. 9 is an example of a pouch 906 containing a smokeable material, fitted in a vaporization device 900. In this example, the device comprises a body 901. The device may comprise a mouthpiece 902 with an aerosol outlet 922, a condenser 903, a heater 905, and an oven or vaporization region 904. The oven region 904 may comprise an oven or vaporization chamber 907. Air may be drawn into the device through the air inlet 921 by a user puffing on the mouth piece. The pouch 906 may be placed in the oven region 904, where it may be heated by the heater 905 to generate a vapor or aerosols of the smokeable material. The pouch may comprise a permeable material or a thermally conductive material with a perforation pattern. Permeability of the pouch by means of composition of a permeable material or perforations may improve heat and mass transfer to the smokeable material in the pouch (e.g., eliminate the need for aeration vents in the oven region 904).

[0075] FIG. 10 shows an example of an oven region 1000 of a device. The oven region may comprise an oven chamber 1007 designed to fit a cartridge comprising a pouch (e.g., a permeable pouch). The pouch may comprise a permeable material or a thermally conductive material with a perforation pattern. The oven chamber may have a lid 1030 so that the user may access the oven region to insert and remove cartridges. Air may be drawn in to the oven region through an inlet 1021 and exit the oven region through an outlet 1022. Vapor generated from the heating of the

smokeable material in the pouch may exit the oven region through an outlet 1022. The air may mix with vapor generated from the heating of the smokeable material. The mixing may take place in the oven chamber 1007, and the combined gas stream may exit through the outlet 1022.

Permeability of the pouch by means of composition of a permeable material or perforations may improve heat and mass transfer to the smokeable material in the pouch (e.g., eliminate the need for aeration vents in the oven region 1000).

[0076] In some implementations, devices comprising a vaporization chamber configured to fit a pouch (e.g., as shown in FIGs. 9 and 10) may advantageously be used with a pouch that is permeable all around. In some examples, more efficient vapor removal may be achieved with an air path that traverses the pouch, as shown in FIGs. 9 and 10. In some implementations, greater flexibility for the device design may be realized as a result of improved air flow and vapor removal. For one example, the air inlet 22 in FIG. 2 may be provided on the mouthpiece 11 in an alternative configuration. In another example, the air inlet may be configured separately from the mouthpiece, as shown, for example, in FIG. 9.

[0077] It is to be understood that the terminology used herein is used for the purpose of describing specific embodiments, and is not intended to limit the scope of the present invention. It should be noted that as used herein, the singular forms of “a”, “an” and “the” include plural references unless the context clearly dictates otherwise. In addition, unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

[0078] While preferable embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS**WHAT IS CLAIMED IS:**

1. A cartridge fitted in a device, the cartridge comprising:
a permeable pouch containing a smokeable material,
wherein the device is configured to heat the smokeable material in the permeable pouch,
and
wherein the permeable pouch allows an exit of a vapor generated from the heating of the smokeable material.
2. The cartridge of claim 1, wherein the permeable pouch comprises cellulose.
3. The cartridge of claim 1, wherein the permeable pouch is capable of withstanding the heating of the smokeable material in the permeable pouch.
4. The cartridge of claim 1, wherein the permeable pouch comprises a binding agent.
5. The cartridge of claim 4, wherein the binding agent is capable of withstanding the heating of the smokeable material in the permeable pouch.
6. The cartridge of claim 1, wherein the permeable pouch is heat-sealed.
7. The cartridge of claim 1, wherein the permeable pouch is air permeable.
8. The cartridge of claim 1, wherein the permeable pouch is vapor permeable.
9. The cartridge of claim 1, wherein the smokeable material comprises a vapor forming medium.
10. The cartridge of claim 9, wherein the vapor forming medium comprises glycerin.
11. The cartridge of claim 1, wherein the device is configured to heat the smokeable material to a temperature required to vaporize the smokeable material.
12. The cartridge of claim 1, wherein the device is configured to heat the cartridge to below about 400 F.
13. The cartridge of claim 1, wherein the cartridge is configured to be inserted into a heated vaporization chamber of the device.
14. The cartridge of claim 1, wherein the smokeable material comprises tobacco.

15. The cartridge of claim 1, wherein the smokeable material comprises botanicals.
16. The cartridge of claim 15, wherein the smokeable material comprises cannabis.
17. The cartridge of claim 1, wherein the smokeable material comprises fine pieces of the smokeable material.
18. The cartridge of claim 1, wherein the smokeable material comprises loose leaves of the smokeable material.
19. The cartridge of claim 1, wherein the permeable pouch encloses the smokeable material on all sides.

1/5

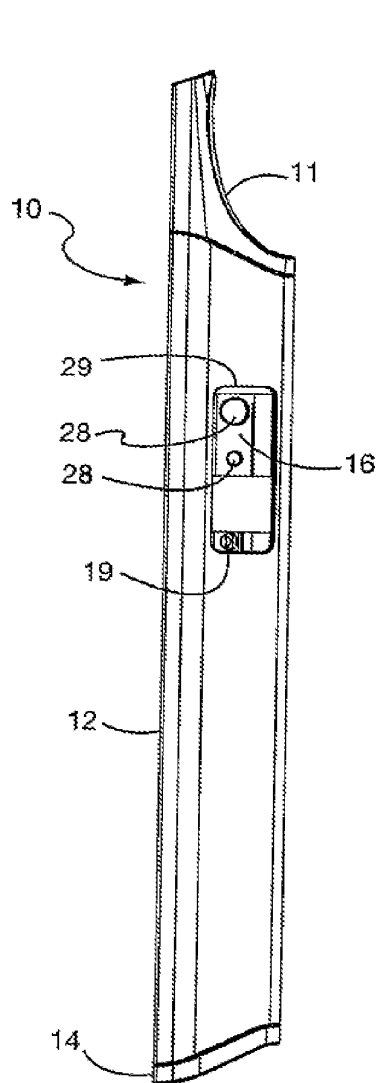


FIG. 1

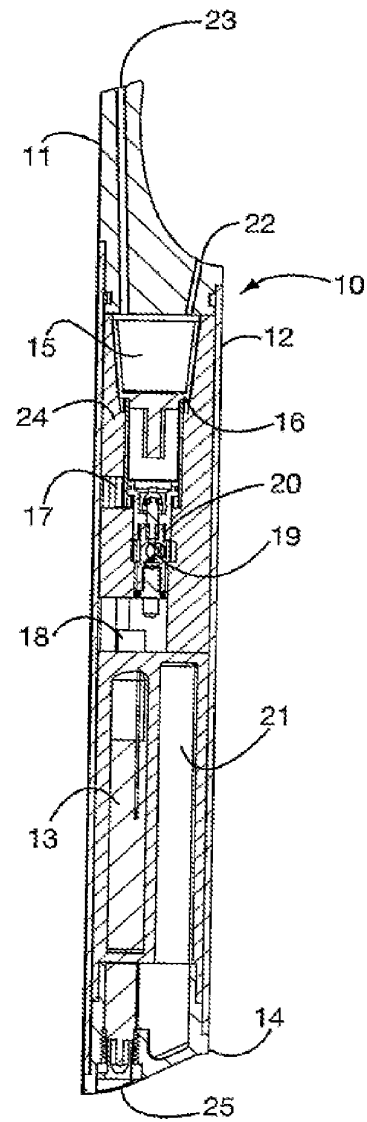
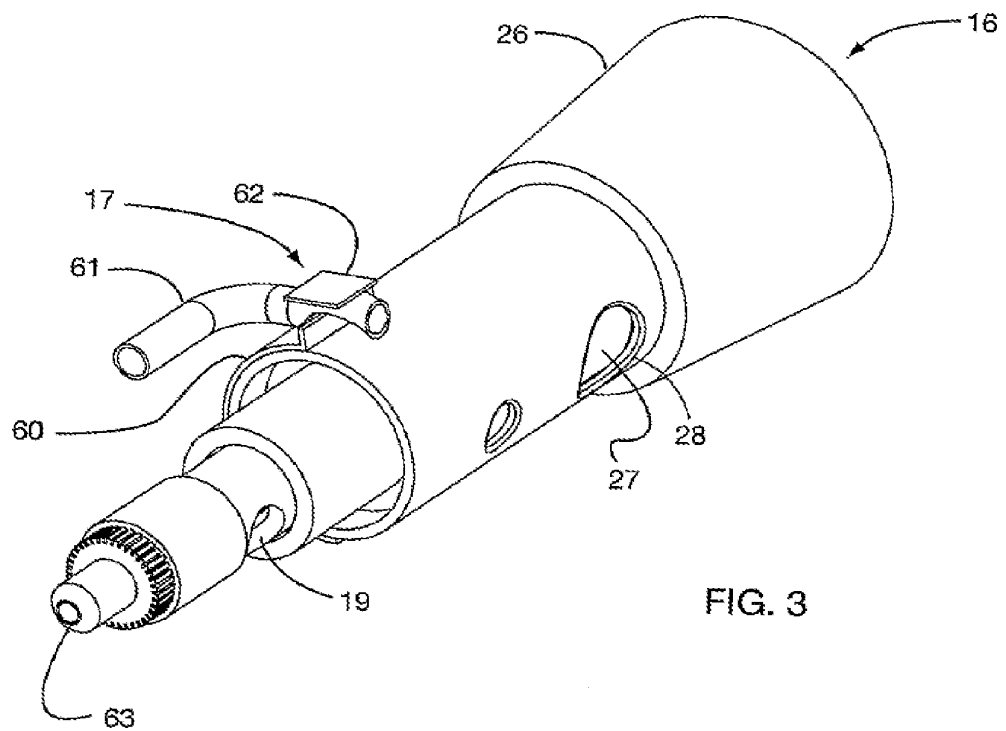
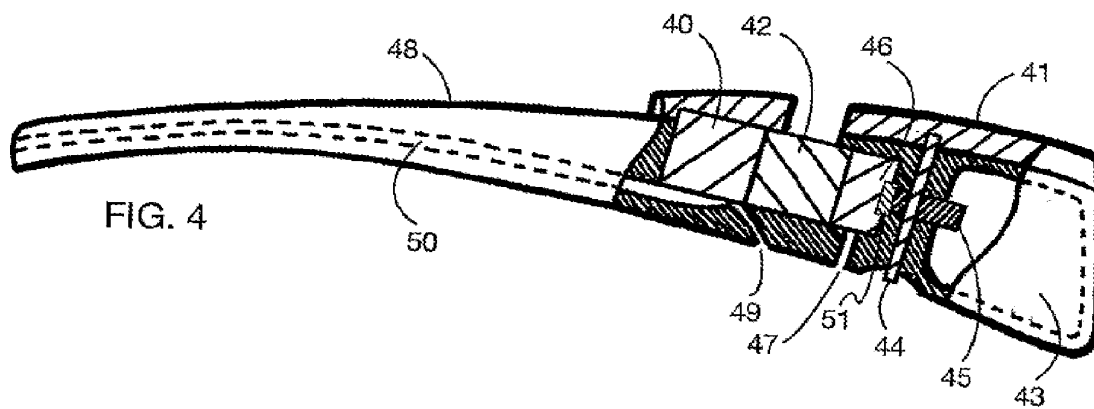


FIG. 2

2/5



3/5

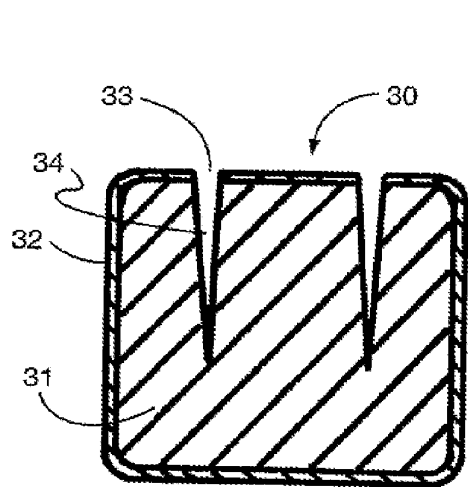


FIG. 5

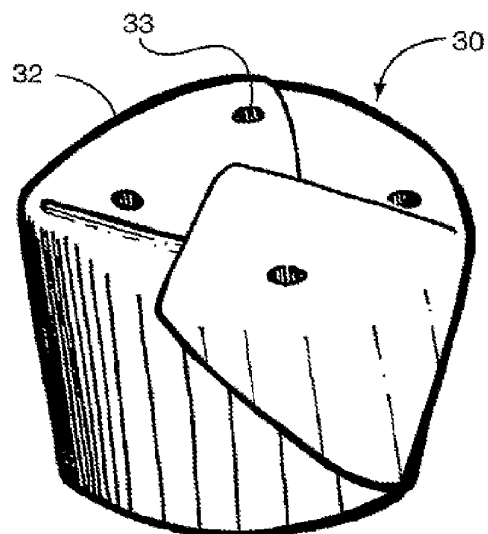


FIG. 6

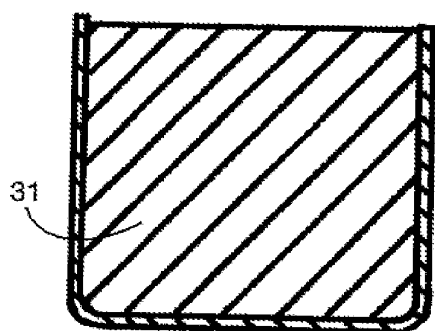


FIG. 7

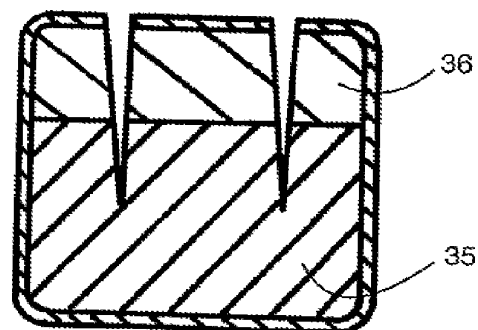


FIG. 8

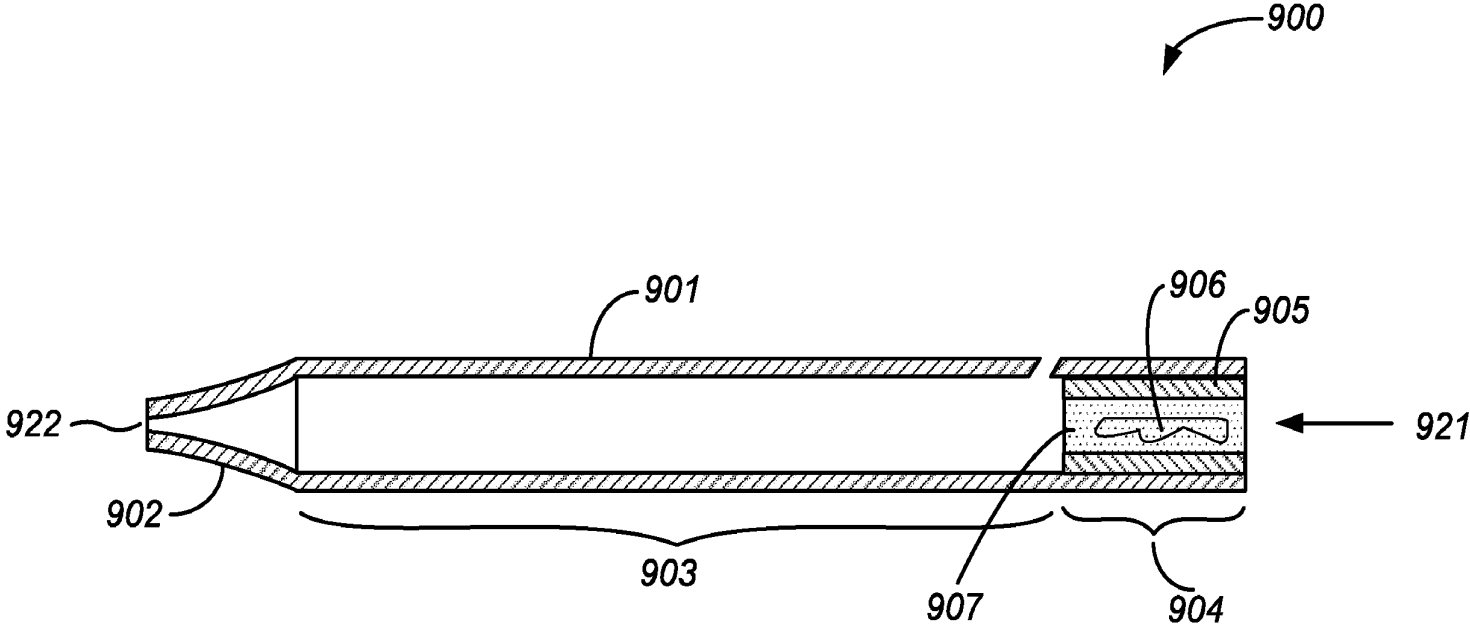
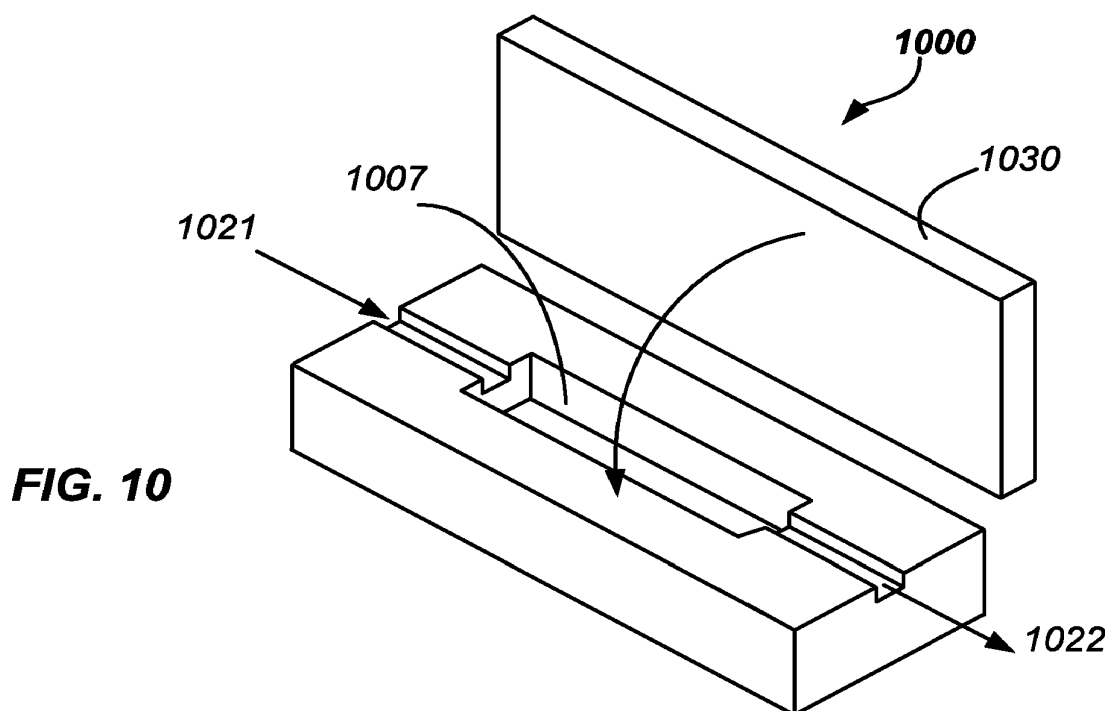


FIG. 9

5/5



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US15/31152

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A24F 23/02 (2015.01) CPC - A24F 23/02 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC(8): A24D 1/14; A24F 13/00, 47/00; A24B 15/16, 15/00 (2015.01); CPC: A24F 13/04, 23/02, 47/004, 47/006, 47/008; A61M 2205/3368, 2205/0266, 11/041, 15/06, 15/0028, 11/048; A24 D1/14; A24B 15/10, 15/165; Y10T 156/1039, 156/1023; B65D 77/04, 9/207 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google/Google Scholar; ProQuest; IP.COM; KEYWORDS: smoking, drag, device, article, appliance, mechanism, permeable, porous, passable, pouch, sachet, pocket, sac, sack, receptacle, binder, binding, cellulose, heat, resistant, seal, air, gas, vapor, glycerin, temperature, chamber, housing, tobacco, botanicals		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0024834 A1 (OGLESBY AP et al.) February 4, 2010; figures 1-3; paragraphs [0045], [0082], [0088], [0091], [0093], [095], [0096], [0122], [0125], [0126], [0127]	1-5, 7-9, 11-15, 17-19
Y		6, 10, 16
Y	US 8,671,952 B2 (WINTERSON WD et al.) March 18, 2014; figure 1; column 3 lines 20-34	6
Y	US 7,726,320 B2 (ROBINSON JH et al.) June 1, 2010; column 16 lines 6-10; column 28 lines 7-18	10
Y	US 8,490,629 B1 (SHENASSA MB et al.) July 23, 2013; abstract; column 1, lines 11-14	16
A	US 5,065,776 A (LAWSON JW et al.) November 19, 1991; entire document	1-19
A	US 2011/0041861 A1 (SEBASTIAN AD et al.) February 24, 2011; entire document	1-19
A	US 3,373,915 A (ANDERSON WE et al.) March 19, 1968; entire document	1-19
A	US 2013/0042865 A1 (MONSEES et al.) February 21, 2013; entire document	1-19
☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 31 July 2015 (31.07.2015)		Date of mailing of the international search report 14 AUG 2015
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300		Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT QSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

Electronic Acknowledgement Receipt

EFS ID:	25213043
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	16-MAR-2016
Filing Date:	28-OCT-2015
Time Stamp:	14:20:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	WO2014187770A2.pdf	1996472	no	29
			95d18139b6c97de4d596c214a2350293e6d54c06		
Warnings:					
Information:					

2	Foreign Reference	WO2015006652A1.pdf	3520366	no	74
			f5e8ae815018e0b78579051aac298084aac e898		
Warnings:					
Information:					
3	Foreign Reference	WO2015040180A2.pdf	1559547	no	28
			5140731366310f120c4eb5a07dc1befebff1 12bf		
Warnings:					
Information:					
4	Foreign Reference	WO2015082652A1.pdf	1000555	no	19
			38d3d280f701a43c92f3674e0613c274ce9c 1f02		
Warnings:					
Information:					
5	Foreign Reference	WO2015084544A1.pdf	5708151	no	96
			c729a79e36c588d51c358d8a2c5051009d4 fc060		
Warnings:					
Information:					
6	Foreign Reference	WO2015101651A1.pdf	1921727	no	33
			bf1134ae94cc5a88aca71c27ffb1e9a971c7f 73b		
Warnings:					
Information:					
7	Foreign Reference	WO2015124878A1.pdf	1336991	no	38
			f2bfc1e32fbbedd0fb8fadca37d2b4576b376 09f4		
Warnings:					
Information:					
8	Foreign Reference	WO2015148547A1.pdf	1438191	no	40
			5b2a6c6a43b3afe40ecee71e8616fedc543b d6a3		
Warnings:					
Information:					
9	Foreign Reference	WO2015175979A1.pdf	1119240	no	23
			0dd652d7668462d8e3d3db8ac6c821153f7 6a199		
Warnings:					
Information:					
10	Non Patent Literature	ECF- AnyInterestInDeterminingNicotine.pdf	945899	no	8
			f45d4738ac20cd0f4cfda305be518eb16c45 56ce		
Warnings:					
Information:					

11	Non Patent Literature	Bombick_et_al- Part2ChemicalAndBiological. pdf	478386	no	8
			14ab76e4ed74bdec4d3e3071a6ad5df4c6421cdc		
Warnings:					
Information:					
12	Non Patent Literature	Bombick_et_al- Part3ChemicalAndBiological. pdf	392773	no	7
			5fa2131a60b3a540bbc3e44e70466aec6b1d8385		
Warnings:					
Information:					
13	Non Patent Literature	Borgerding_et_al- Part1ChemicalAndBiological. pdf	1370908	no	13
			fd584d757c9d92460d2fcd4ddde06d50b5a8a34ca		
Warnings:					
Information:					
14	Non Patent Literature	Mirriam-Webster_Lighter.pdf	217877	no	2
			f7c501314ae49e09f1fbf39a5ba2e80245b35dc6		
Warnings:					
Information:					
15	Non Patent Literature	Baker_et_al- ThePyrolysisOfTobacco.pdf	2879309	no	89
			4b0893691633ed9d79e393be947f5f87354315b5		
Warnings:					
Information:					
16	Non Patent Literature	Torikai_et_al- EffectOfTemperature.pdf	711044	no	9
			6bddde6d5e43171f769eed5db35224f150206102e		
Warnings:					
Information:					
17	Non Patent Literature	Ward-GreenLeafThreshing.pdf	1277487	no	7
			b28df6ab57bb5892d621fa45fb6d06e65361d3a0		
Warnings:					
Information:					
18	Non Patent Literature	Ingebrethsen_et_al- ElectronicCigaretteAerosol.pdf	878285	no	9
			9adfa01d50eceb11167a85a8d4a1358640f3d752		
Warnings:					
Information:					
19	Non Patent Literature	McCann_et_al- DetectionOfCarcinogens.pdf	589865	no	5
			2c765bee4e459ebc6a924f04ff346bd9923c85f5		
Warnings:					
Information:					

20	Non Patent Literature	Wells-GlycerinAsAConstituent.pdf	400896 55e15a965e5197a0ada0588565d1024ad9fd2e01	no	7
Warnings:					
Information:					
21	Non Patent Literature	Kuo_et_al-AppendixDParticleSize.pdf	118553 bd6edf7f6957d7459bbfb02198723c3f321c8596	no	3
Warnings:					
Information:					
22	Non Patent Literature	HarvestVapour-AmericanBlendTobacco.pdf	192959 aa2d2ce86dbb83eaaeb0defe2b01175fc928da9e	no	2
Warnings:					
Information:					
23	Non Patent Literature	INCHEM-LevulinicAcid-Mar2003.pdf	38840 696c8649b74fe2ad08053b5ad55ed838a8a081cb	no	1
Warnings:					
Information:					
24	Non Patent Literature	INCHEM-BenzoicAcid-May2005.pdf	73915 e2fb66054fa0822703fa47b589f6ac3442871681	no	2
Warnings:					
Information:					
25	Non Patent Literature	FoodAndDrugAdministration-TheCompoundingPharmacy.pdf	279626 415c15baSceff8c9d29cfcf15e295ff317e5f752	no	3
Warnings:					
Information:					
26	Non Patent Literature	INCHEM-PyruvicAcid-Jan2003.pdf	33530 7371b9d02c93cafe786924332b0f6ee89b7a6475	no	1
Warnings:					
Information:					
27	Non Patent Literature	INCHEM-SorbicAcid-May2005.pdf	53872 57875ff939c0f0b06c9f35643f5c751691e2d16	no	1
Warnings:					
Information:					
28	Non Patent Literature	Flouris_et_al-AcuteImpactOfActive.pdf	1250365 0edc97cbd42bb7257ff60febd681ff100c9d6dc	no	12
Warnings:					
Information:					

29	Non Patent Literature	Goniewicz_et_al- NicotineLevelsInElectronic.pdf	785815 93f15bd1715bdf7fc9a2652cca5774ec1e9ff715	no	9
Warnings:					
Information:					
30	Non Patent Literature	Seeman_et_al- TheFormOfNicotine.pdf	1326537 b591d90db200c24ab2b64f48266210d4da82fc58	no	13
Warnings:					
Information:					
31	Non Patent Literature	Vansickel_et_al- AClinicalLaboratory.pdf	759955 df7d5b89aecdd44cdc34a84ccc7a3b315de4aae75	no	9
Warnings:					
Information:					
32	Non Patent Literature	Zhang_et_al- InVitroParticleSize.pdf	625228 e1cbf9ec3cb441b965b7a2fb3424a796b2b5c4a9	no	8
Warnings:					
Information:					
33	Non Patent Literature	Nicoli_et_al- MammalianTumorXenografts. pdf	1881086 01dec3636aa89952d4ada56f48082fea27ec89a	no	5
Warnings:					
Information:					
34	Non Patent Literature	YouTube- FireflyVaporizorReview.pdf	128746 19ccc5a77bdfaca05e07ddee58a341f6fb28ec7	no	1
Warnings:					
Information:					
35	Non Patent Literature	Perfetti_StructuralStudyNicotineSalts_1983.pdf	1995767 2c689cfbc458ce980fd57948bada4be583c1e834	no	12
Warnings:					
Information:					
Total Files Size (in bytes):			39288763		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8
I hereby certify that this correspondence is being transmitted to
the USPTO via EFS-Web on March 16, 2016.

/Mary Buggie/ 3/16/2016
Mary Buggie Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
First Named Inventor : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
AND METHODS THEREOF
Customer No. : 66854

AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION

This reply is in response to the non-final Office Action mailed December 16, 2015 for which a response is due March 16, 2016, and is therefore timely filed. The Commissioner is hereby authorized to charge any fees to make this filing timely to Deposit Account No. 50-4050 and to credit any overpayments to Deposit Account No. 50-4050.

Amendments to the Claims are shown in the listing of claims that begins on page 2.

Interview Summary begins on page 6.

Remarks begin on page 7.

Reconsideration and allowance of the pending claims, in light of the amendments and remarks presented herein is respectfully requested.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of delivering nicotine to a user comprising:
deploying ~~an electronic cigarette~~ a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, ~~an organic~~ lactic acid, and a biologically acceptable liquid carrier, wherein:
 - a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - ~~b. the nicotine formulation comprises nicotine lactate;~~
 - ~~[c.]~~b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and
 - ~~[d.]~~c. operation of the ~~electronic cigarette~~ low-temperature vaporizer comprises heating at least a portion of the nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C;wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
2. (Original) The method of claim 1, wherein a molar ratio of nicotine to organic acid is between about 1:1 and 1:3.
3. (Original) The method of claim 1, wherein the nicotine formulation further comprises at least one flavorant.
4. (Original) The method of claim 1, wherein the nicotine concentration is about 4.5%.
5. (Cancelled)

6. (Original) The method of claim 1, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
7. (Currently amended) A method of delivering nicotine to a user comprising:
deploying ~~an electronic cigarette~~ a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, ~~a carboxylic acid, wherein the carboxylic acid comprises~~ lactic acid, and a biologically acceptable liquid carrier, wherein:
- a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the nicotine formulation comprises protonated nicotine;
 - c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol;
 - d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the ~~electronic cigarette-low-temperature vaporizer~~; and
 - e. operation of the ~~electronic cigarette-low-temperature vaporizer~~ comprises heating at least a portion of the nicotine formulation between about 100°C and 300°C to generate an inhalable aerosol;
wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
8. (Original) The method of claim 7, wherein a molar ratio of nicotine to organic acid is between 1:1 and 1:3.
9. (Original) The method of claim 7, wherein the nicotine formulation further comprises at least one flavorant.
10. (Original) The method of claim 7, wherein the nicotine concentration is about 4.5%.
11. (Cancelled)

12. (Original) The method of claim 7, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
13. (Currently amended) ~~An electronic cigarette~~ A low-temperature vaporizer, comprising:
a liquid reservoir;
a nicotine formulation within the liquid reservoir, the nicotine formulation comprising:
 nicotine lactate;
 propylene glycol; and
 90%-30% vegetable glycerol;
wherein a concentration of nicotine in the nicotine formulation is from about 0.5% (w/w)
 to about 20% (w/w);
a vaporizing component configured to produce an aerosol from the nicotine formulation
 by heating at least a portion of the nicotine formulation between 100°C and 300°C;
and
a mouthpiece configured to connect to the reservoir for inhalation of the aerosol;
wherein inhalation of the aerosol into the user's lungs over a period of about 5 minutes at
 a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from
 about 3 min to about 8 min and further wherein the user may modify the amount of
 nicotine delivered by adjusting inhalation strength.
14. (Original) The electronic cigarette of claim 13, further comprises a battery configured to provide power to the vaporizing component.
15. (Original) The electronic cigarette of claim 13, wherein a molar ratio of nicotine to organic acid is between 1:1 and 1:3.
16. (Original) The electronic cigarette of claim 13, wherein the nicotine formulation further comprises at least one flavorant.
17. (Original) The electronic cigarette of claim 13, wherein the vaporizing component comprises a heating element in fluid communication with the nicotine formulation.

18. (Original) The electronic cigarette of claim 13, wherein the nicotine concentration is about 4.5%.

19. (Cancelled)

20. (Original) The electronic cigarette of claim 13, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.

INTERVIEW SUMMARY

Applicants thank the Examiner for the courtesies extended during the telephone interview of March 10, 2016. During the interview Applicants discussed the amendments made herein in light of the cited prior art, as discussed below. Agreement was reached that these amendments would overcome the cited art, although the Examiner indicated that further searching would need to be performed.

REMARKS

Claims 1-20 were pending. No claims were previously withdrawn from consideration, and no claims had been previously cancelled. By this response, claims 1, 7 and 13 have been amended, claims 5, 11 and 19 have been cancelled, and no claims have been added. Support for these amendments, and for any new claims, may be found throughout the specification, but especially in paragraphs [110], [112], [113], [115], [121] and [132]. Cancellation or amendment of any claim is not to be considered a dedication to the public of any subject matter.

Thus, claims 1-4, 6-10, 12-18 and 20 are currently under consideration.

DOUBLE PATENTING

Claims 1-12

Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 9,215,895 to Bowen et al. ("Bowen '895") in view of U.S. Patent Application Publication No. 2014/0261474 to Igor Gonda ("Gonda").

By this response, claims 1-12 have been amended. Upon an indication that the claims are otherwise allowable, should the Examiner maintain the rejection of claims 1-12 for double patenting over Bowen '895 and Gonda, Applicants will likely file a terminal disclaimer, as suggested by the Examiner. In light of the amendments to the claims, a terminal disclaimer at this point would be premature.

Claims 1-4, 6-10 and 12

Claims 1-4, 6-10 and 12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 105-122 of copending U.S. Patent Application No. 14/271,071.

By this response, claims 1-4, 6-10 and 12 have been amended. Upon an indication that the claims are otherwise allowable, should the Examiner maintain the rejection of claims 1-4, 6-

10 and 12 for double patenting over copending U.S. Patent Application No. 14/271,071, Applicants will likely file a terminal disclaimer, as suggested by the Examiner. In light of the amendments to the claims, a terminal disclaimer at this point would be premature.

Claims 5 and 11

Claims 5 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 105-122 of copending U.S. Patent Application No. 14/271,071 in view of Gonda and U.S. Patent Application Publication No. 2009/0151717 to Bowen et al. ("Bowen'717").

By this response, claims 5 and 11 have been cancelled, though their subject matter has been incorporated into the independent claims. Upon an indication that the claims are otherwise allowable, should the Examiner maintain the rejection of the claims for double patenting over Bowen '717, Applicants will likely file a terminal disclaimer, as suggested by the Examiner. In light of the amendments to the claims, a terminal disclaimer at this point would be premature.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-4, 7-10 and 13-18

Claims 1-4, 7-10 and 13-18 currently stand rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent Application Publication No. 2006/0196518 to Lik Hon ("Hon") in view of Gonda.

The Applicants respectfully disagree.

The combination of Hon and Gonda does not suggest all of the features of claims 1-4, 7-10 and 13-18. In addition, the combination of Hon with Gonda in the manner suggested by the Office Action of December 16, 2016 is improper because it relies on impermissible hindsight.

As described in the Applicants' specification and discussed during the telephone interview of March 10, 2016, the claimed invention solves a long standing problem in the field electronic cigarettes --- that is, how to convincingly mimic the experience of a traditional

cigarette using a nicotine vaporizer --- by applying previously unrecognized discoveries. Specifically, the Applicants have discovered that some, but not all, nicotine salts, when properly formulated, may produce a nicotine plasma concentration (C_{max}) and time course (T_{max}) that most closely resembles that of traditional cigarettes. Further, when formulated as recited in the claims, including formulating in between 30%-90% vegetable glycerol and a glycol (such as propylene glycol), the user experience is surprisingly similar in “taste” and “feel”, and therefore overall satisfaction, to that of a traditional cigarette. Importantly, when using other nicotine salts and other formulations, the user experience is not sufficiently similar to that of a traditional cigarette.

The Applicants’ instant claims are directed in particular, to one particular nicotine salt, present in a solution of nicotine (e.g., freebase nicotine) and lactic acid in a biologically acceptable liquid carrier including propylene glycol and 90%-30% vegetable glycerol. This nicotine salt formulation, when vaporized using a low-temperature vaporizer between about 100°C and 300°C, results in a user experience that closely mimics a traditional cigarette even within the first 3-8 minutes of inhaling. The combination of nicotine and lactic acid in the carrier including propylene glycol and 90%-30% vegetable glycerol for use in a low-temperature vaporization device operating between 100°C and 300°C is based, in part, on the Applicants’ unique discovery that only certain nicotine salts (e.g., and therefore only certain organic acids forming these salts) have a nicotine C_{max} and T_{max} in blood plasma of a user inhaling the vapor that is similar to that of inhaling smoke from a traditional cigarette. For example, the Applicants’ disclosure (see, e.g., figures 1-5 and accompanying description) describes for the first time the plasma T_{max} and C_{max} of a variety of nicotine formulations, and teaches which formulations (and specifically which nicotine salts) do and do not have this desired effect.

As will be described in greater detail below, without the Applicant’s teachings, one of skill in the art would not be motivated to provide a nicotine formulation and method of using it as described herein, and therefore it would not be obvious to combine references, including the Hon and Gonda references raised by the Office Action of December 16, 2015.

A. The combination of Hon and Gonda does not suggest all of the features of the claims.

The combination of Hon and Gonda does not suggest all of the features recited by the pending claims including claims 1-4, 7-10 and 13-18. Specifically, the combination of Hon and Gonda does not suggest: (1) a low-temperature vaporization device or a method of using a low-temperature vaporizing device *wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min*; (2) a low-temperature vaporizer or a method of using a *low-temperature vaporizer* to heat a nicotine formulation *to generate an inhalable aerosol between about 100°C and about 300°C*; (3) a low-temperature vaporizer device or a method of using a low-temperature vaporizer device to heat a nicotine solution *including a biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol*; or (4) a low-temperature vaporization device *wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength*.

First, the combination of Hon and Gonda does not suggest a low-temperature vaporization device or a method of using a low-temperature vaporizing device wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min. Hon and Gonda are silent as to the Tmax profiles of any of the nicotine formulations described in either Hon or Gonda. Further, it would not be obvious to modify the combination of Hon and Gonda to include this feature. Applicants note that this limitation was originally present in dependent claims 5, 11 and 19, but has now been included in each of the independent claims. In the Office Action of December 16, 2015, the Hon and Gonda were combined with Bowen et al. (US patent App. Pub. 2009/0151717, hereafter "Bowen '717"). The Office Action argues that this feature would be obvious, because the "collective disclosure [of Hon, Gonda and Bowen '717] indicates that the parameter of pH, aerosolized nicotine particle size and even nicotine concentration in the liquid formulation and inhalation rate are all 'results-effective variables'..." As such, only routine experimentation would be needed to optimize these variables to achieve the "recognized result" (see. Office Action, page 10), and therefore it would be obvious to one of ordinary skill "to have undergone routine experimentation and fabricated the nicotine formulation of Hon in the form of a liquid nicotine lactate salt solution and, in so

doing, arrived at the claimed particle size and inhalation rate which result in the claimed Tmax parameters...”

Applicants disagree. In order to be obvious for optimization, a variable must be first recognized as a results-effective variable in the prior art. See, e.g., *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In this case, neither the result (e.g., that the Tmax of nicotine in the plasma was between 3 and 8 minutes) nor the variables that Applicants have shown critically effect this result (e.g., the type of nicotine salt), are known in the prior art, and therefore it could not be obvious to optimize. Applicant point out that, as described in the Applicants’ specification for the first time, the type of nicotine salt and therefore the organic acid used to form the salt in the formulation, is critical to achieving the recited Tmax. The variables cited by the Office Action in reference to Gonda (e.g., pH, particle size, nicotine concentration) are irrelevant if the wrong acid and therefore salt is generated, as described in the Applicants’ specification (e.g., see paragraph [115] “... not all nicotine salts perform similarly to each other or to a traditional cigarette with respect to the rate of nicotine uptake in the blood at early time periods (0-1.5 minutes). These results are unexpected.”). Without knowing what variables must be optimized (e.g., which acid and therefore nicotine salt to use), it could not be obvious to optimize the combination of Hon and Gonda, which each described a laundry list of acids and nicotine salts, including many that could not be optimized as recited in the claims.

Second, the combination of Hon and Gonda does not suggest a low-temperature vaporizer or a method of using a low-temperature vaporizer to heat a nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C. Hon describes only “high temperature vaporization.” See, e.g., Hon, abstract (“high temperature vaporization nozzle”, [006] (“a high temperature vaporization nozzle”), [021] (“the nicotine solution is then vaporized into high temperature vapor”), and [025] (“vaporized and condensed subsequently to form a puff of smoke at high temperature”). Gonda does not apply heat to form the vapor, but describes instead the use of a filter. Thus, the combination of Hon and Gonda does not suggest a low-temperature vaporizer or a method of using one.

Third, the combination of Hon and Gonda does not suggest a low-temperature vaporizer device or a method of using a low-temperature vaporizer device to heat a nicotine solution

including a biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol. Hon describes only propylene glycol content of between 80%-90% (where the “rest is glycerol”, Hon, paragraph [020]). Similarly, Gonda suggests only that “Glycerin and glycols have been also used in inhalation products.” Gonda, paragraph [078]. Neither reference alone or in combination suggests the combination of propylene glycol and 90%-30% vegetable glycerol.

Finally, the combination of Hon and Gonda does not suggest a low-temperature vaporization device wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength. Both Hon and Gonda are metered delivery devices in which the amount of material applied per puff is metered or determined by the device. In Hon, the dose of nicotine vapor is applied by spraying the high-temperature vapor that is actively pumped out of the electronic cigarette. See, e.g., Hon, paragraph [006] (“...an electronic pump or a valve connected with a metering cavity...”). Similarly in Gonda, the device partitions the volume inhaled into parts, so that vapor including nicotine is delivered as a bolus only during a portion of the inhalation. See, e.g., Gonda paragraph [021] and [094], which is taught as being important in controlling the rate of entry of nicotine to the blood and/or brain. Gonda, paragraph [025]. Neither Hon nor Gonda, nor the combination of the two, are configured to modify the amount of nicotine delivered by adjusting the inhalation strength.

B. Impermissible Hindsight is required to modify Hon (or Gonda) to obviate the pending claims.

It would not be obvious to modify Hon, Gonda, or the combination of Hon and Gonda to include all of the features recited in the claims, at least because this modification would require the knowledge found only in the Applicant’s disclosure, which is impermissible hindsight. Specifically, the Applicants’ instant claims are directed to a particular nicotine salt formulation, present in a solution of nicotine (e.g., freebase nicotine) and lactic acid in a biologically acceptable liquid carrier including propylene glycol and 90%-30% vegetable glycerol. It was Applicant’s unique finding that only certain nicotine salt formulations, (including this one) when vaporized using a low-temperature vaporizer between about 100°C and 300°C, results in a user experience that closely mimics a traditional cigarette and produces a nicotine Tmax within the

first 3-8 minutes of inhaling. Thus, combination of nicotine and lactic acid in the carrier including propylene glycol and 90%-30% vegetable glycerol for use in a low-temperature vaporization device operating between 100°C and 300°C is based, in part, on the Applicants' unique discovery that only certain nicotine salts (e.g., and therefore only certain organic acids forming these salts) have a nicotine Tmax in blood plasma of that is similar to that of inhaling smoke from a traditional cigarette.

Applicants respectfully submit that the combination of Hon and Gonda is improper because the Office Action relies on information gleaned solely from Applicant's specification. In this case, The Office Action is incorrect in suggesting that it would be obvious to modify Hon to include lactic acid from Gonda. Hon mentions only the use of a nicotine mixture "including an organic acid" and describes as an example of the organic acid only citric acid. Gonda mentions a long list of organic acids that may be combined with nicotine, including lactic acid, but also include many others, including many (such as citric acid) that do not produce a nicotine Tmax within the first 3-8 minutes of inhaling. It is only the Applicant's teaching of which acids and resulting nicotine salts, particularly in the context of a mixture of propylene glycol and 90%-30% vegetable glycerol, which result in the recited features, including the unexpected result of producing a plasma nicotine Tmax of between 3 and 8 minutes. It is only the Applicants' own teaching that suggests the use of lactic acid with a solution of nicotine having a concentration from about 0.5% (w/w) to about 20% (w/w) in a carrier of propylene glycol and 90%-30% vegetable glycerol to produce a nicotine Tmax of 3-8 minutes.

MPEP § 2142 states that "impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art" Any judgment on obviousness "is, in a sense, necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper" (MPEP § 2145(X)(A), quoting *In re McLaughlin*, 443 F.2d 1392, 1395 (CCPA 1971).

In the present case, the Office Action argues that it would be obvious to modify Hon to include lactic acid because "the Gonda reference teaches that administering an aerosolized,

liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to effectuate a peak level of nicotine in the blood plasma after a very short time period – mimicking that which is typically achieved during actual cigarette smoking – is known.” However, this is not accurate. The prior art, Gonda included, did not realize that the some, but not all, nicotine salt formulations result in a peak (Tmax) blood plasma level within 3-8 minutes. This information was known only to the Applicants. Instead, Gonda taught that peak nicotine concentration was set only by the concentration, particle size, and pH which effect the deposition profile in the user’s airway. Gonda, as indeed all of the prior art, was not aware that the type of nicotine salt (and therefore the included acid) was important, and therefore could provide no guidance suggesting which acid and resulting salt from those known in the art (including those listed by Gonda) would work, or what formulation of this acid and nicotine would work. It was only the Applicant’s teaching that provides this suggestion.

As discussed in detail in the Applicants’ specification, some, but not all, nicotine nicotine salts and formulations of nicotine salts have the recited property of producing a nicotine Tmax within 3-8 minutes, and providing a user experience that mimic’s traditional cigarettes. See, e.g., paragraphs [111], [114], and Example 6. Due to the lack of suggestion in the prior art to this effect, and the fact that this discovery is only present on the record in Applicant’s specification, it logically follows that this suggestion has been improperly gleaned from Applicant’s own specification and that the combination of Hon and Gonda (with or without Bowen’717) is an exercise of impermissible hindsight. Accordingly, it is respectfully submitted that the combination is improper and respectfully requested that the rejection be withdrawn.

Since the combination of Hon and Gonda does not suggest all of the features of claims 1-4, 7-10 and 13-18, and since the combination of Hon and Gonda to include even some of these features requires the use of impermissible hindsight, these claims cannot be obvious in light of these references. Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection of claims 1-4, 7-10 and 13-18 and allowance of all of the currently pending claims.

Claims 5-6, 11-12 and 19-20

Claims 5-6, 11-12 and 19-20 currently stand rejected under 35 U.S.C. § 103 as being unpatentable over Hon in view of Gonda and Bowen '717.

The Applicants respectfully disagree.

Bowen '717 cannot cure the deficiencies discussed above. As already discussed above, the combination of Hon, Gonda and Bowen '717 does not suggest the recited formulation, and specifically does not suggest, without the use of hindsight based on the Applicant's disclosure: (1) a low-temperature vaporization device or a method of using a low-temperature vaporizing device *wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min*; (2) a low-temperature vaporizer or a method of using a low-temperature vaporizer to heat a nicotine formulation *to generate an inhalable aerosol between about 100°C and about 300°C*; (3) a low-temperature vaporizer device or a method of using a low-temperature vaporizer device to heat a nicotine solution *including a biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol*; or (4) a low-temperature vaporization device *wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength*.

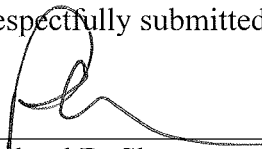
Since the combination of Hon, Gonda and Bowen '717 does not suggest all of the features recited in the claims, these claims cannot be obvious in light of these references. The Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection of claims 5-6, 11-12 and 19-20, and allowance of the currently pending claims.

CONCLUSION

Applicants respectfully request that the Examiner expedite the prosecution of this patent application to issuance. If the Patent Office determines that an extension of time and/or other relief is required, Applicants petition for any required relief including extension of time, and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-4050**, referencing 13211-713.303. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Date: March 16, 2016

Respectfully submitted,



Richard D. Shoop
Reg. No. 45,763

SHAY GLENN LLP
2755 CAMPUS DRIVE, SUITE 210
SAN MATEO, CA 94403
TELEPHONE: 650.287.2186
FACSIMILE: 650.212.7562

Electronic Acknowledgement Receipt

EFS ID:	25219659
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Mary Buggie
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	16-MAR-2016
Filing Date:	28-OCT-2015
Time Stamp:	19:41:31
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_Response_NFO A_3-16-2016.pdf	751188	yes	16
			c6ed14172f0008fba12e51031548c83095c f687		

Multipart Description/PDF files in .zip description			
Document Description		Start	End
Amendment/Req. Reconsideration-After Non-Final Reject		1	1
Claims		2	5
Applicant summary of interview with examiner		6	6
Applicant Arguments/Remarks Made in an Amendment		7	16

Warnings:

Information:

Total Files Size (in bytes):	751188
-------------------------------------	--------

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/925,968	Filing Date 10/28/2015	☐ To be Mailed
---	---	----------------------------------	---------------------------------------

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (j), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X \$ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X \$ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)
	03/16/2016	CLAIMS REMAINING AFTER AMENDMENT					
	Total (37 CFR 1.16(i))	* 17	Minus	** 20	= 0	X \$80 =	0
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)
		CLAIMS REMAINING AFTER AMENDMENT					
	Total (37 CFR 1.16(i))	*	Minus	**	=	X \$ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X \$ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/STELLA LITTLE/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P. O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/925,968	10/28/2015	Adam BOWEN	13211-713.303	2707
66854	7590	03/17/2016		
SHAY GLENN LLP 2755 CAMPUS DRIVE SUITE 210 SAN MATEO, CA 94403			EXAMINER MAYES, DIONNE WALLS	
			ART UNIT	PAPER NUMBER
			1747	
			NOTIFICATION DATE	DELIVERY MODE
			03/17/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@shayglenn.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 14/925,968	Applicant(s) BOWEN ET AL.	
	Examiner DIONNE WALLS MAYES	Art Unit 1747	

All participants (applicant, applicant's representative, PTO personnel):

(1) DIONNE WALLS MAYES. (3) ADAM BOWEN.

(2) RICHARD SHOOP. (4) _____.

Date of Interview: 10 March 2016.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☐Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: Those of Record.

Identification of prior art discussed: Hon (2006/0196518) and Gonda (2014/0261474).

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicants Representative, Mr. Shoop, and Inventor, Mr. Bowen, presented proposed amendments to the instant claims along with arguments supporting their position that the claims now clearly define over the prior art of record, sepcifically Hon and Gonda. Examiner Mayes indicated that while she could not definitively indicate that the proposed claims would be allowable, she did believe Applicant's arguments to be strong and would consider them favorably, in addition to performing an updated prior art search. Applicant indicated a quick response to the outstanding Office Action would be filed .

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/DIONNE WALLS MAYES/ Examiner, Art Unit 1747	
---	--

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Electronic Acknowledgement Receipt

EFS ID:	25583557
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Kathleen R. Kelleher/Brian Flick
Filer Authorized By:	Kathleen R. Kelleher
Attorney Docket Number:	13211-713.303
Receipt Date:	25-APR-2016
Filing Date:	28-OCT-2015
Time Stamp:	12:43:23
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_4-25-2016.pdf	272362	yes	4
			bee2683fa11dca624f97df95db9ce37b0c0511cc		

Multipart Description/PDF files in .zip description			
Document Description		Start	End
Transmittal Letter		1	3
Information Disclosure Statement (IDS) Form (SB08)		4	4

Warnings:

Information:

Total Files Size (in bytes):	272362
-------------------------------------	--------

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on 4-25-2016.

Brian Fleck
 Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
 First Named Inventor : Adam Bowen
 Filed : October 28, 2015
 Art Unit : 1747
 Examiner : Mayes, Dionne Walls
 Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
 AND METHODS THEREOF
 Customer No. : 66854

INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT

☐ **37 CFR §1.97(b)**

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ **1).** Within 3 months of the application filing date, or
☐ **2).** Within 3 months of entry of a national stage as set forth in § 1.491, or
☐ **3).** Before the mail date of a first Office Action on the merits, or
☐ **3a).** Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
☐ **4).** Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
☐ **4a).** Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☒ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☒ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☐ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☒ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☐ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under § 1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement

--AND--

B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☒ **37 CFR § 1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☒ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☐ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☐ **37 CFR § 1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ 3). A copy of each application specification is not submitted because the application is stored in the IFW. Cite no(s):

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☐ **37 CFR § 1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☐ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

- ☐ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**
- ☐ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**
- ☐ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☐ 2a). An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): **--AND/OR--**
- ☐ 2b). A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): **--OR--**
- ☐ 3). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

STATEMENT UNDER 37 CFR § 1.97(e)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement.
- ☒ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

STATEMENT UNDER 37 CFR § 1.704(d)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

- ☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$0.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

Dated: 4/25/16

By: Kathleen R. Kelleher, Reg. No. 62,230

Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854

13211-713.303

Electronic Acknowledgement Receipt

EFS ID:	25762843
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Kathleen R. Kelleher/Brian Flick
Filer Authorized By:	Kathleen R. Kelleher
Attorney Docket Number:	13211-713.303
Receipt Date:	12-MAY-2016
Filing Date:	28-OCT-2015
Time Stamp:	15:52:01
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_5-1 2-2016.pdf	271221	yes	4
			f5873d971498ec862ff4262dafec35d259f9ded1		

Multipart Description/PDF files in .zip description			
Document Description		Start	End
Transmittal Letter		1	3
Information Disclosure Statement (IDS) Form (SB08)		4	4

Warnings:

Information:

Total Files Size (in bytes):	271221
-------------------------------------	--------

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on 5-12-2016.Brian T. Lee
Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
 First Named Inventor : Adam Bowen
 Filed : October 28, 2015
 Art Unit : 1747
 Examiner : Mayes, Dionne Walls
 Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
 AND METHODS THEREOF
 Customer No. : 66854

INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and /or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT

☐ **37 CFR §1.97(b)**

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ 1). Within 3 months of the application filing date, or
☐ 2). Within 3 months of entry of a national stage as set forth in § 1.491, or
☐ 3). Before the mail date of a first Office Action on the merits, or
☐ 3a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
☐ 4). Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
☐ 4a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☒ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☒ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☐ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☒ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☐ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under § 1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement

--AND--

B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☒ **37 CFR § 1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☒ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☐ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☐ **37 CFR § 1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ 3). A copy of each application specification is not submitted because the application is stored in the IFW. Cite no(s):

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☐ **37 CFR § 1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☐ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

- ☐ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**
- ☐ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**
- ☐ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☐ 2a). An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): **--AND/OR--**
- ☐ 2b). A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): **--OR--**
- ☐ 3). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date: .

STATEMENT UNDER 37 CFR § 1.97(e)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement.
- ☒ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

STATEMENT UNDER 37 CFR § 1.704(d)

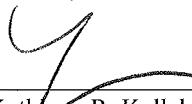
- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

- ☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$0.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

Dated: 5/12/16

By: 
Kathleen R. Kelleher, Reg. No. 62,230

Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P. O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/925,968	10/28/2015	Adam BOWEN	13211-713.303	2707
66854	7590	05/13/2016		
SHAY GLENN LLP 2755 CAMPUS DRIVE SUITE 210 SAN MATEO, CA 94403			EXAMINER MAYES, DIONNE WALLS	
			ART UNIT	PAPER NUMBER
			1747	
			NOTIFICATION DATE	DELIVERY MODE
			05/13/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@shayglenn.com

Office Action Summary	Application No. 14/925,968	Applicant(s) BOWEN ET AL.	
	Examiner DIONNE WALLS MAYES	Art Unit 1747	AIA (First Inventor to File) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/16/2016.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

- 5) ☒ Claim(s) 1-4,6-10,12-18 and 20 is/are pending in the application.
5a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1-4,6-10,12-18 and 20 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

- a) ☐ All b) ☐ Some** c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
Paper No(s)/Mail Date ____.
- 3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 4) ☐ Other: ____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Rejections - 35 USC § 112

2. The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2, 8 and 15 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Each of the above-recited claims recite the phrase “organic acid”; however, because of the amendments to the claims, filed on March 16, 2016, there is now insufficient antecedent basis for this limitation in the claims.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least

one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit <http://www.uspto.gov/forms/>. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to <http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp>.

5. Claims 1-4, 6-10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-15 of Bowen '895 (U.S. Patent No. 9,215,895) in view of Griffith, Jr. et al (US. Pat. App. Pub. 2013/0255702).

Regarding the instant independent claim 1, the Bowen '895 patent claims recites a method of delivering nicotine to a user comprising deploying an electronic cigarette comprising a nicotine formulation which comprises nicotine, an acid and a biologically acceptable carrier, wherein inhalation of the aerosol is formed by heating the nicotine formulation and inhaling it into the user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma $T_{\max}$ from about 3 min to about 8 min. Bowen '895 fails, however, to recite that the electronic cigarette is a "low-temperature" one which operates by heating the nicotine formulation to between about 100-300 degrees C, wherein the nicotine formulation comprises nicotine in combination with the specific acid of lactic acid and the specific biologically acceptable carrier of propylene glycol and 90%-30% glycerol. However, the Griffith, Jr. et al reference teaches a low temperature electronic cigarette operating at the claimed temperature ranges to heat a nicotine formulation which also includes lactic acid, and a glycerin/90-30% glycerol solution (see paras.[0014],[0019],[0086]-[0088]). Hence, it would have been obvious to one having ordinary skill in the art to have included the nicotine formulation of Griffith, Jr. et al, operating at the designated temperatures, in the device of Bowen '895 as such is already known in the art.

Regarding claim 2, Griffith, Jr. et al discloses that its nicotine formulation can include about 0.5 moles of lactic acid per one mole of nicotine (see para. [0086]), so it

would have been obvious to one having ordinary skill in the art to have chosen this molar ratio for the Bowen '895 nicotine formulation.

Regarding claim 3, it would have been obvious to one having ordinary skill in the art to have added a flavorant to the modified nicotine formulation in order to enhance the organoleptic quality of the same for the benefit of the user.

Regarding claim 4, independent claim 1 of Bowen '925 recites a nicotine concentration of between 2% to 6% (w/w).

Regarding claim 6, independent claim 1, Bowen '925 recites a nicotine formulation that generates an aerosol comprising particles sizes from about 0.1 microns to about 5 microns.

Regarding the instant independent claim 7, the Bowen '895 patent claims recites a method of delivering nicotine to a user comprising deploying an electronic cigarette comprising a nicotine formulation which comprises nicotine, an acid and a biologically acceptable carrier, wherein inhalation of the aerosol is formed by heating the nicotine formulation and inhaling it into the user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma $T_{\max}$ from about 3 min to about 8 min. The nicotine may not be disclosed as being "protonated", but given that it is provided in a carrier with lactic acid, it follows that a nicotine salt (i.e., nicotine lactate) would be formed, thus rendering the nicotine "protonated". Further, it fails, however, to recite that the electronic cigarette is a "low-temperature" one which operates by heating the nicotine formulation to between about 100-300 degrees C, wherein the nicotine formulation comprises nicotine in combination with the specific acid

of lactic acid and the specific biologically acceptable carrier of propylene glycol and 90%-30% glycerol. However, the Griffith, Jr. et al reference teaches a low temperature electronic cigarette operating at the claimed temperature ranges to heat a nicotine formulation which also includes lactic acid, and a glycerin/90-30% glycerol solution (see paras.[0014],[0019],[0086]-[0088]). Hence, it would have been obvious to one having ordinary skill in the art to have included the nicotine formulation of Griffith, Jr. et al, operating at the designated temperatures, in the device of Bowen '895 as such is already known in the art.

Regarding claim 8, Griffith, Jr. et al discloses that its nicotine formulation can include about 0.5 moles of lactic acid per one mole of nicotine (see para. [0086]), so it would have been obvious to one having ordinary skill in the art to have chosen this molar ratio for the Bowen '895 nicotine formulation.

Regarding claim 9, it would have been obvious to one having ordinary skill in the art to have added a flavorant to the modified nicotine formulation in order to enhance the organoleptic quality of the same for the benefit of the user.

Regarding claim 10, independent claim 1 of Bowen '925 recites a nicotine concentration of between 2% to 6% (w/w).

Regarding claim 12, independent claim 1, Bowen '925 recites a nicotine formulation that generates an aerosol comprising particles sizes from about 0.1 microns to about 5 microns.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102 of this title, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims the examiner presumes that the subject matter of the various claims was commonly owned as of the effective filing date of the claimed invention(s) absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and effective filing dates of each claim that was not commonly owned as of the effective filing date of the later invention in order for the examiner to consider the applicability of 35 U.S.C. 102(b)(2)(C) for any potential 35 U.S.C. 102(a)(2) prior art against the later invention.

9. Claims 1-4, 6-10, 12-18 and 20 are rejected under 35 U.S.C. 103 as being unpatentable over Griffith, Jr. et al (US. Pat. App. Pub. 2013/0255702) - as evidenced

by www.e-cigarette-forum.com's PG-VG-PEG Discussion Posting (hereinafter referred to as "the PG-VG-PEG Internet Posting") - in view of Gonda (US. Pat. No. 2014/0261474) and Bowen '717 et al (US. Pat. App. Pub. 2009/0151717).

Regarding independent claim 1, Griffith, Jr. et al discloses an aerosol delivery article, and its use, for yielding materials in an inhalable form. Specifically, Griffith, Jr. et al discloses the oral delivery of inhalable materials comprising a resistive heating element formed of a substrate wherein an electrically conductive material is integrally formed with a carrier material that can be coated or impregnated with materials that can be aerosolized for inhalation, i.e. aerosol precursor material. The aerosol precursor can comprise any materials that are volatilizable at the disclosed working temperatures (ranging from 50-300 degrees C), an example of which is 75-80% by weight glycerol (Note: "The PG-VG-PEG Internet Posting" serves as evidence that the terms "glycerol" and "vegetable glycerol/glycerin" are synonymous), 1-10% by weight propylene glycol, 2-3% by weight nicotine and 0.1-0.5% by weight of one or more flavors. Griffith, Jr. et al also discloses that an organic acid (such as lactic acid) can be added as the "flavor" in said aerosol precursor (see paras.[0009], [0014],[0019],[0086]-[0088])(corresponding to the claimed "A method of delivering nicotine to a user comprising: deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier, wherein: a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w); b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and c. operation of the

low-temperature vaporizer comprises heating at least a portion of the nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C”).

Griffith, Jr. et al is silent as to the peak amount and timeframe of nicotine delivery into a user's bloodstream upon inhalation of its aerosolized materials. However, the Gonda reference teaches that administering an aerosolized, liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to effectuate a peak level of nicotine in the blood plasma after a very short period of time - mimicking that which is typically achieved during actual cigarette smoking - can be accomplished. Specifically, Gonda teaches that a nicotine formulation in solution, can be prepared so as to be inhaled to emulate the effects of smoking wherein the aerosol is delivered in a relatively small volume at the beginning of a puff and a low puff rate to enhance deposition and rapid absorption in the lungs which results in rapid delivery of nicotine. (see paras. [0043], [0052], [0064], [0067], [0078], [0091]-[0092]). Also, Gonda states that adjustments in pH, in combination with changing the particle size of the aerosol, can be carried out to create a different experience for the user. For example, by decreasing the pH of the nicotine formulation, the likelihood of airway irritation and cough is reduced, and/or by decreasing the particle size of the inhaled material, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels (see para. [0007],[0033]-[0036], [0052], [0064], [0086]). Further, Gonda states that, during inhalation of aerosolized nicotine formulations, a satisfactory dose of nicotine is achieved in a small number of breaths, spaced by short periods, preferably

less than 2 minutes (see para. [0017]). (Note: To this point, the Bowen '717 et al reference further discloses that, typically, when smokers "puff" on cigarettes they may take a puff every 30 seconds (i.e., in an intense smoking regime. Bowen '717 et al then shows that aerosol devices used to inhale a nicotine substance can also be "smoked" in such manner (see para. [0107])). The afore-mentioned *collective* disclosure indicates that the parameters of pH, aerosolized nicotine particle size, nicotine concentration in the liquid formulation and even inhalation rate, are all "result-effective variables". Once a particular parameter is recognized as a result-effective variable, i.e., a variable which achieves a recognized result, the determination of the optimum or workable ranges of said variable can be characterized by routine experimentation. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) MPEP 2144.05. Hence, it would have been obvious to one having ordinary skill in the art at the time of the invention to have undergone routine experimentation and fabricated the nicotine formulation of Griffith, Jr. et al in the form of a liquid nicotine solution and, in so doing, arrived at the claimed inhalation rate which result in the claimed $T_{\max}$ parameters, after determining that these values provided, as close as possible, the same nicotine blood levels achieved by smoking a conventional cigarette. Hence, it would have been obvious to one having ordinary skill in the art to have operated the device of Griffith, Jr. et al such that it delivers nicotine to a user per the teachings of Gonda in order to achieve the benefits described above (corresponding to the claimed "wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma $T_{\max}$ from about 3 minutes to about 8 min and

further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength”).

Regarding claim 2, Griffith, Jr. et al discloses that its aerosol precursor can include about 0.5 moles of lactic acid per one mole of nicotine (see para. [0086])(corresponding to the claimed “wherein a molar ratio of nicotine to organic acid is between about 1:1 and 1:3”)

Regarding claim 3, Griffith, Jr. et al discloses that its aerosol precursor material can be combined with more than one flavorant (see para. [0049])(corresponding to the claimed “wherein the nicotine formulation further comprises at least one flavorant”).

Regarding claim 4, Griffith, Jr. et al discloses that a specific non-limiting example of the nicotine content in its aerosol precursor may be about 2-3% by weight (see para. [00888]). However, it would have been obvious to one having ordinary skill in the art to have adjusted this amount to be a bit higher - corresponding to the claimed amount - in order to satisfy the particular organoleptic preferences of the user (corresponding to the claimed “wherein the nicotine concentration is about 4.5%”).

Regarding claim 6, based on the disclosure of Gonda, as discussed above, that by decreasing the particle size, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels, it would have been obvious to one having ordinary skill in the art to have optimized the particle size of its aerosol to fall between 0.1 - 5 microns (Corresponding to the claimed “wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns”).

Regarding independent claim 7, Griffith, Jr. et al discloses an aerosol delivery article, and its use, for yielding materials in an inhalable form. Specifically, Griffith, Jr. et al discloses the oral delivery of inhalable materials comprising a resistive heating element formed of a substrate wherein an electrically conductive material is integrally formed with a carrier material that can be coated or impregnated with materials that can be aerosolized for inhalation, i.e. aerosol precursor material. The aerosol precursor can comprise any materials that are volatilizable at the disclosed working temperatures (ranging from 50-300 degrees C), an example of which is 75-80% by weight glycerol, 1-10% by weight propylene glycol, 2-3% by weight nicotine and 0.1-0.5% by weight of one or more flavors. Griffith, Jr. et al also discloses that an organic acid (such as lactic acid) can be added as the "flavor" in said aerosol precursor (Note: The nicotine of Griffith, Jr. et al may not be disclosed as being "protonated", but given that it is provided in a carrier with lactic acid, it is reasonable to presume that a nicotine salt (i.e., nicotine lactate) would be formed in the solution, thus rendering the nicotine "protonated")(see paras.[0009], [0014],[0019],[0086]-[0088])(corresponding to the claimed "A method of delivering nicotine to a user comprising: deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier, wherein: a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w); b. the nicotine formulation comprises protonated nicotine; c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the low temperature vaporizer;

and e. operation of the low-temperature vaporizer comprises heating at least a portion of the nicotine formulation between about 100 °C and about 300 °C to generate an inhalable aerosol”).

Griffith, Jr. et al is silent as to the peak amount and timeframe of nicotine delivery into a user's bloodstream upon inhalation of its aerosolized materials. However, the Gonda reference teaches that administering an aerosolized, liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to effectuate a peak level of nicotine in the blood plasma after a very short period of time - mimicking that which is typically achieved during actual cigarette smoking - can be accomplished. Specifically, Gonda teaches that a nicotine formulation in solution, can be prepared so as to be inhaled to emulate the effects of smoking wherein the aerosol is delivered in a relatively small volume at the beginning of a puff and a low puff rate to enhance deposition and rapid absorption in the lungs which results in rapid delivery of nicotine. (see paras. [0043], [0052], [0064], [0067], [0078], [0091]-[0092]). Also, Gonda states that adjustments in pH, in combination with changing the particle size of the aerosol, can be carried out to create a different experience for the user. By decreasing the pH of the nicotine formulation, the likelihood of airway irritation and cough is reduced. By decreasing the particle size of the inhaled material, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels (see para. [0007],[0033]-[0036], [0052], [0064], [0086]). Further, Gonda states that, during inhalation of aerosolized nicotine formulations, a satisfactory dose of nicotine is achieved in a small number of

breaths, spaced by short periods, preferably less than 2 minutes (see para. [0017]).

(Note: To this point, the Bowen '717 et al reference further discloses that, typically, when smokers "puff" on cigarettes they may take a puff every 30 seconds (i.e., in an intense smoking regime. Bowen '717 et al then shows that aerosol devices used to inhale a nicotine substance can also be "smoked" in such manner (see para. [0107])).

The afore-mentioned *collective* disclosure indicates that the parameters of pH, aerosolized nicotine particle size, nicotine concentration in the liquid formulation and even inhalation rate, are all "result-effective variables". Once a particular parameter is recognized as a result-effective variable, i.e., a variable which achieves a recognized result, the determination of the optimum or workable ranges of said variable can be characterized by routine experimentation. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) MPEP 2144.05. Hence, it would have been obvious to one having ordinary skill in the art at the time of the invention to have undergone routine experimentation and fabricated the nicotine formulation of Griffith, Jr. et al in the form of a liquid nicotine solution and, in so doing, arrived at the claimed inhalation rate which result in the claimed $T_{\max}$ parameters, after determining that these values provided, as close as possible, the same nicotine blood levels achieved by smoking a conventional cigarette. Hence, it would have been obvious to one having ordinary skill in the art to have operated the device of Griffith, Jr. et al such that it delivers nicotine to a user per the teachings of Gonda in order to achieve the benefits described above (corresponding to the claimed "wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine

plasma $T_{\max}$ from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength”).

Regarding claim 8, Griffith, Jr. et al discloses that its aerosol precursor can include about 0.5 moles of lactic acid per one mole of nicotine (see para. [0086])(corresponding to the claimed “wherein a molar ratio of nicotine to organic acid is between about 1:1 and 1:3”)

Regarding claim 9, Griffith, Jr. et al discloses that its aerosol precursor material can be combined with more than one flavorant (see para. [0049])(corresponding to the claimed “wherein the nicotine formulation further comprises at least one flavorant”).

Regarding claim 10, Griffith, Jr. et al discloses that a specific non-limiting example of the nicotine content in its aerosol precursor may be about 2-3% by weight (see para. [00888]). However, it would have been obvious to one having ordinary skill in the art to have adjusted this amount to be a bit higher - corresponding to the claimed amount - in order to satisfy the particular organoleptic preferences of the user (corresponding to the claimed “wherein the nicotine concentration is about 4.5%”).

Regarding claim 12, based on the disclosure of Gonda, as discussed above, that by decreasing the particle size, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels, it would have been obvious to one having ordinary skill in the art to have optimized the particle size of its aerosol to fall between 0.1 - 5 microns (Corresponding to the claimed “wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns”).

Regarding independent claim 13, Griffith, Jr. et al discloses an aerosol delivery article (10) for yielding materials in an inhalable form having a mouth-end (11) with an opening (18) to allow for withdrawal of an aerosol, from an inside cavity, which has been vaporized by a resistive heating element (50) that heats an aerosol precursor material loaded on a substrate (53). The aerosol precursor can comprise any materials that are volatilizable at the disclosed working temperatures (ranging from 50-300 degrees C), an example of which is 75-80% by weight glycerol, 1-10% by weight propylene glycol, 2-3% by weight nicotine and 0.1-0.5% by weight of one or more flavors. Griffith, Jr. et al also discloses that an organic acid (such as lactic acid) can be added as the "flavor" in said aerosol precursor (Note: The nicotine of Griffith, Jr. et al may not be disclosed as also being in the form of its salt "nicotine lactate", but given that it is provided in a carrier with lactic acid, it is reasonable to presume that the nicotine salt (i.e., nicotine lactate) would be formed in the solution (see paras.[0009], [0014],[0019],[0086]-[0088],[0137])(corresponding to the claimed "A low-temperature vaporizer comprising a liquid reservoir; a nicotine formulation within the liquid reservoir, the nicotine formulation comprising: nicotine lactate; propylene glycol; and 90%-30% vegetable glycerol; wherein the concentration of nicotine in the nicotine formulation is from about 0.5% (w/w) to about 20%(w/w); a vaporizing component configured to produce an aerosol from the nicotine formulation by heating at least a portion of the nicotine formulation between 100 degrees C and 300 degrees C; and a mouthpiece configured to connect to the reservoir for inhalation of the aerosol").

Griffith, Jr. et al is silent as to the peak amount and timeframe of nicotine delivery into a user's bloodstream upon inhalation of its aerosolized materials. However, the Gonda reference teaches that administering an aerosolized, liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to effectuate a peak level of nicotine in the blood plasma after a very short period of time - mimicking that which is typically achieved during actual cigarette smoking - can be accomplished. Specifically, Gonda teaches that a nicotine formulation in solution, can be prepared so as to be inhaled to emulate the effects of smoking wherein the aerosol is delivered in a relatively small volume at the beginning of a puff and a low puff rate to enhance deposition and rapid absorption in the lungs which results in rapid delivery of nicotine. (see paras. [0043], [0052], [0064], [0067], [0078], [0091]-[0092]). Also, Gonda states that adjustments in pH, in combination with changing the particle size of the aerosol, can be carried out to create a different experience for the user. By decreasing the pH of the nicotine formulation, the likelihood of airway irritation and cough is reduced. By decreasing the particle size of the inhaled material, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels (see para. [0007],[0033]-[0036], [0052], [0064], [0086]). Further, Gonda states that, during inhalation of aerosolized nicotine formulations, a satisfactory dose of nicotine is achieved in a small number of breaths, spaced by short periods, preferably less than 2 minutes (see para. [0017]). (Note: To this point, the Bowen '717 et al reference further discloses that, typically, when smokers "puff" on cigarettes they may take a puff every 30 seconds (i.e., in an

intense smoking regime. Bowen '717 et al then shows that aerosol devices used to inhale a nicotine substance can also be "smoked" in such manner (see para. [0107])). The afore-mentioned *collective* disclosure indicates that the parameters of pH, aerosolized nicotine particle size, nicotine concentration in the liquid formulation and even inhalation rate, are all "result-effective variables". Once a particular parameter is recognized as a result-effective variable, i.e., a variable which achieves a recognized result, the determination of the optimum or workable ranges of said variable can be characterized by routine experimentation. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) MPEP 2144.05. Hence, it would have been obvious to one having ordinary skill in the art at the time of the invention to have undergone routine experimentation and fabricated the nicotine formulation of Griffith, Jr. et al in the form of a liquid nicotine solution and, in so doing, arrived at the claimed inhalation rate which result in the claimed $T_{\max}$ parameters, after determining that these values provided, as close as possible, the same nicotine blood levels achieved by smoking a conventional cigarette. Hence, it would have been obvious to one having ordinary skill in the art to have operated the device of Griffith, Jr. et al such that it delivers nicotine to a user per the teachings of Gonda in order to achieve the benefits described above (corresponding to the claimed "wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma $T_{\max}$ from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength").

Regarding claim 14, the aerosol delivery article of Griffith, Jr. et al may include a battery (40)(see Fig. 1, para. [0134])(corresponding to the claimed “further comprises a battery configured to provide power to the vaporizing component”).

Regarding claim 15, Griffith, Jr. et al discloses that its aerosol precursor can include about 0.5 moles of lactic acid per one mole of nicotine (see para. [0086])(corresponding to the claimed “wherein a molar ratio of nicotine to organic acid is between about 1:1 and 1:3”)

Regarding claim 16, Griffith, Jr. et al discloses that its aerosol precursor material can be combined with more than one flavorant (see para. [0049])(corresponding to the claimed “wherein the nicotine formulation further comprises at least one flavorant”).

Regarding claim 17, as stated above, Griffith, Jr. et al discloses that the aerosol, from an inside cavity, is vaporized by a resistive heating element (50) that heats the nicotine-containing aerosol precursor material located on a substrate (53)(see para. [0137])(corresponding to the claimed “wherein the vaporizing component comprises a heating element in fluid communication with the nicotine formulation”).

Regarding claim 18, Griffith, Jr. et al discloses that a specific non-limiting example of the nicotine content in its aerosol precursor may be about 2-3% by weight (see para. [00888]). However, it would have been obvious to one having ordinary skill in the art to have adjusted this amount to be a bit higher - corresponding to the claimed amount - in order to satisfy the particular organoleptic preferences of the user (corresponding to the claimed “wherein the nicotine concentration is about 4.5%”).

Regarding claim 20, based on the disclosure of Gonda, as discussed above, that by decreasing the particle size, the aerosolized particles of nicotine will deposit deeper in the lungs, which increases the rate of absorption of the nicotine and leads to an increase in peak nicotine plasma levels, it would have been obvious to one having ordinary skill in the art to have optimized the particle size of its aerosol to fall between 0.1 - 5 microns (Corresponding to the claimed "wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns").

Response to Arguments

10. Applicant's arguments with respect to the claims have been considered but are moot in view of the new grounds for rejection, presented above, involving a new combination of prior art references, which were necessitated because of the amendments made to the claims, filed on March 16, 2016.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DIONNE WALLS MAYES whose telephone number is (571)272-5836. The examiner can normally be reached on Tuesday and Thursday, 8:00A - 6:30P EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael H. Wilson can be reached on 571-270-3882. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DIONNE WALLS MAYES/
Examiner, Art Unit 1747

/MICHAEL H WILSON/
Supervisory Patent Examiner, Art Unit 1747

Notice of References Cited	Application/Control No. 14/925,968		Applicant(s)/Patent Under Reexamination BOWEN ET AL.	
	Examiner DIONNE WALLS MAYES		Art Unit 1747	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-2013/0255702 A1	10-2013	Griffith, Jr. et al.	A24F47/008	131/328
	B	US-				
	C	US-				
	D	US-				
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	E-Cigarette Forum - PG-VG-PEG Discussion Posting - https://www.e-cigarette-forum.com/forum/threads/pg-vg-peg.177551/ , dated April 8, 2011.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes 	Application/Control No. 14925968	Applicant(s)/Patent Under Reexamination BOWEN ET AL.
	Examiner DIONNE W MAYES	Art Unit 1747

CPC- SEARCHED		
Symbol	Date	Examiner
a24f47/00; a24f47/008	4/27/2016	DWM

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
EAST Search conducted (see attached search strategy)	12/10/2015	DWM
Inventor search conducted	12/10/2015	DWM
EAST Search conducted (see attached search strategy)	4/27/2016	DWM
Inventor search updated	4/27/2016	DWM

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

--	--

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 1 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	1	US- 374,584	12/13/1887	Cook	
	2	US- 576,653	2/9/1897	Bowlby	
	3	US- 595,070	12/7/1897	Oldenbusch	
	4	US- 720,007	2/10/1903	Dexter	
	5	US- 799,844	9/19/1905	Fuller	
	6	US- 968,160	8/23/1910	Johnson	
	7	US- 969,076	8/30/1910	Pender	
	8	US- 1,067,531	7/15/1913	MacGregor	
	9	US- 1,163,183	12/7/1915	Stoll	
	10	US- 1,299,162	4/1/1919	Fisher	
	11	US- 1,505,748	8/19/1924	Louis	
	12	US- 1,552,877	9/8/1925	Phillipps et al.	
	13	US- 1,632,335	6/14/1927	Hiering	
	14	US- 1,706,244	3/19/1929	Louis	
	15	US- 1,845,340	2/16/1932	Ritz	
	16	US- 1,972,118	9/4/1934	McDill	
	17	US- 1,998,683	4/23/1935	Montgomery	
	18	US- 2,031,363	2/18/1936	Elof	
	19	US- 2,039,559	5/5/1936	Segal	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	374	CA2641869A1	5/6/2010	Xia, Hao Ran		
	375	CN101869356A(w/EngTrans)	10/27/2010	Liu Zheqi		
	376	CN102754924A(w/EngTrans)	10/31/2012	Long		
	377	CN1122213A(w/EngAbs)	5/15/1996	Philip Morris Prod Inc		
	378	CN85106876A(w/EngCorres)	9/3/1986	M. J. Luinoziancaogose		
	379	DE19854005A1(w/EngAbs)	5/18/2000	Reemtsma GmbH		

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 2 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	20	US- 2,104,266	1/4/1938	McCormick	
	21	US- 2,231,909	2/18/1941	Hempel	
	22	US- 2,327,120	8/17/1943	McCoon	
	23	US- 2,460,427	2/1/1949	Musselman et al.	
	24	US- 2,483,304	9/27/1949	Rudolf	
	25	US- 2,502,561	4/4/1950	Ludwig	
	26	US- 2,765,949	10/9/1956	Swan	
	27	US- 2,830,597	4/15/1958	Jakob	
	28	US- 2,860,638	11/18/1958	Frank	
	29	US- 2,897,958	8/4/1959	Tarleton et al.	
	30	US- 2,935,987	5/10/1960	Ackerbauer	
	31	US- 3,146,937	9/1/1964	Joseph	
	32	US- 3,258,015	6/28/1966	Drummond et al.	
	33	US- 3,292,634	12/20/1966	Beucler	
	34	US- 3,373,915	3/19/1968	Anderson et al.	
	35	US- 3,420,360	1/7/1969	Young	
	36	US- 3,479,561	11/18/1969	Janning	
	37	US- 3,567,014	3/2/1971	Feigelman	
	38	US- 3,707,017	12/26/1972	Paquette	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	380	DE19854012A1(w/EngTrans)	5/18/2000	Reemtsma GmbH		
	381	DE4200639A1(w/EngEquiv)	7/23/1992	Brown & Williamson Tob.		
	382	EP0532194A1	3/17/1993	Philip Morris Prod Inc		
	383	EP0535695A2	4/7/1993	Phillips Petroleum Co		
	384	EP1458388A(asWO03/055486)	9/22/2004	McNeil AB		
	385	EP2325093B1	6/20/2012	Imperial Tobacco Ltd		

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents, at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 3 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	39	US- 3,792,704	2/19/1974	Parker	
	40	US- 3,861,523	1/21/1975	Fountain et al.	
	41	US- 3,941,300	3/2/1976	Troth	
	42	US- 4,020,853	5/3/1977	Nuttall	
	43	US- 4,049,005	9/20/1977	Hernandez et al.	
	44	US- 4,066,088	1/3/1978	Ensor	
	45	US- 4,207,976	6/17/1980	Herman	
	46	US- 4,215,708	8/5/1980	Bron	
	47	US- 4,219,032	8/26/1980	Tabatznik et al.	
	48	US- 4,506,683	3/26/1985	Cantrell et al.	
	49	US- 4,519,319	5/28/1985	Howlett	
	50	US- 4,595,024	6/17/1986	Greene et al.	
	51	US- 4,708,151	11/24/1987	Shelar	
	52	US- 4,735,217	4/5/1988	Gerth et al.	
	53	US- 4,771,796	9/20/1988	Myer	
	54	US- 4,793,365	12/27/1988	Sensabaugh Jr. et al.	
	55	US- 4,794,323	12/27/1988	Zhou et al.	
	56	US- 4,798,310	1/17/1989	Kasai et al.	
	57	US- 4,813,536	3/21/1989	Willis	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	386	EP2609821A1	7/3/2013	Philip Morris Prod S.A		
	390	ES2118034A1(w/EngAbs)	9/1/1998	Nugar Bobinajes SI		
	391	GB1025630A	4/14/1966	British American Tobacco		
	392	GB1065678A	4/19/1967	Super Temp Corp		
	393	IE-S2005-0051	2/2/2005	Oglesby & Butler R&D Ltd		
	394	IE-S2005-0563	8/24/2005	Oglesby & Butler R&D Ltd		

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 4 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	58	US- 4,819,665	4/11/1989	Roberts et al.	
	59	US- 4,830,028	5/16/1989	Lawson et al.	
	60	US- 4,836,224	6/6/1989	Lawson et al.	
	61	US- 4,846,199	7/11/1989	Rose	
	62	US- 4,848,374	7/18/1989	Chard et al.	
	63	US- 4,848,563	7/18/1989	Robbins	
	64	US- 4,893,639	1/16/1990	White	
	65	US- 4,907,606	3/13/1990	Lilja et al.	
	66	US- 4,941,483	7/17/1990	Ridings et al.	
	67	US- 4,944,317	7/31/1990	Thal	
	68	US- 4,947,874	8/14/1990	Brooks et al.	
	69	US- 4,947,875	8/14/1990	Brooks et al.	
	70	US- 5,005,759	4/9/1991	Bouche	
	71	US- 5,020,548	6/4/1991	Farrier et al.	
	72	US- 5,027,836	7/2/1991	Shannon et al.	
	73	US- 5,050,621	9/24/1991	Creighton et al.	
	74	US- 5,060,671	10/29/1991	Counts et al.	
	75	US- 5,065,776	11/19/1991	Lawson et al.	
	76	US- 5,076,297	12/31/1991	Farrier et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	395	IE-S2005-0615	9/19/2005	Oglesby & Butler R&D Ltd		
	396	JP02-145179A(w/EngEquiv)	6/4/1990	Hercules Inc		
	397	JP03-049671(w/EngEquiv)	3/4/1991	Brown & Williamson Tob.		
	398	JP03-180166(w/EngEquiv)	8/6/1991	R J Reynolds Tobacco Co		
	399	JP09-075058(w/EngAbs)	3/25/1997	Nagai, Masaya		
	400	JP11-178563(w/EngAbs)	7/6/1999	Japan Tobacco Inc		

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 5 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	77	US- 5,105,831	4/21/1992	Banerjee et al.	
	78	US- 5,105,838	4/21/1992	White et al.	
	79	US- 5,123,530	6/23/1992	Lee	
	80	US- 5,144,962	9/8/1992	Counts et al.	
	81	US- 5,183,062	2/2/1993	Clearman et al.	
	82	US- 5,224,498	7/6/1993	Deevi et al.	
	83	US- 5,249,586	10/5/1993	Morgan et al.	
	84	US- 5,261,424	11/16/1993	Sprinkel Jr.	
	85	US- 5,269,237	12/14/1993	Baker et al.	
	86	US- 5,269,327	12/14/1993	Counts et al.	
	87	US- 5,322,075	6/21/1994	Deevi et al.	
	88	US- 5,324,498	6/28/1994	Streusand et al.	
	89	US- 5,372,148	12/13/1994	McCafferty et al.	
	90	US- 5,388,574	2/14/1995	Ingebrethsen	
	91	US- 5,591,368	1/7/1997	Fleischhauer et al.	
	92	US- 5,605,226	2/25/1997	Hernlein	
	93	US- 5,641,064	6/24/1997	Goserud	
	94	US- 5,649,552	7/22/1997	Cho et al.	
	95	US- 5,666,977	9/16/1997	Higgins et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	401	JP2000-203639(w/EngAbs)	7/25/2000	S & B Foods Inc		
	402	JP2000-236865A(w/EngAbs)	9/5/2000	Seiko Kogyo KK		
	403	JP2001-165437A(w/EngAbs)	6/22/2001	Tsubota Pearl Co Ltd		
	404	JP2005-034021A(w/EngCorres)	2/10/2005	Seiko Epson Corp		
	405	JP2006-504430A(w/EngEquiv)	2/9/2006	R J Reynolds Tobacco Co		
	406	JP62-278975(w/EngAbs)	12/3/1987	Watabe, Isamu		

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
-----------------------	----------------------	--------------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 6 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	96	US- 5,666,978	9/16/1997	Counts et al.	
	97	US- 5,708,258	1/13/1998	Counts et al.	
	98	US- 5,730,118	3/24/1998	Hermanson	
	99	US- 5,730,158	3/24/1998	Collins et al.	
	100	US- 5,746,587	5/5/1998	Racine et al.	
	101	US- 5,810,164	9/22/1998	Rennecamp	
	102	US- 5,819,756	10/13/1998	Mielordt	
	103	US- 5,845,649	12/8/1998	Saito et al.	
	104	US- 5,865,185	2/2/1999	Collins et al.	
	105	US- 5,881,884	3/16/1999	Podosek	
	106	US- 5,931,828	8/3/1999	Durkee	
	107	US- 5,934,289	8/10/1999	Watkins et al.	
	108	US- 5,938,018	8/17/1999	Keaveney et al.	
	109	US- 5,944,025	8/31/1999	Cook et al.	
	110	US- 5,954,979	9/21/1999	Counts et al.	
	111	US- 5,967,310	10/19/1999	Hill	
	112	US- 5,975,415	11/2/1999	Zehnal	
	113	US- 5,979,460	11/9/1999	Matsumura	
	114	US- 5,994,025	11/30/1999	Iwasa et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	407	JP64-37276A(w/EngEquiv)	2/7/1989	R J Reynolds Tobacco Co		
	408	KR0193885B1(w/EngEquiv)	6/15/1999	Philip Morris Prod Inc		
	409	WO95/01137A1	1/12/1995	Voges Innovation Pty Ltd.		
	410	WO97/12639A1	4/10/1997	Slutsky, Arthur		
	411	WO00/28842A1(EngAbs)	5/25/2000	Reemtsma GmbH		
	412	WO03/056948A1(EngAbs)	7/17/2003	Japan Tobacco Inc.		

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 7 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	115	US- 5,996,589	12/7/1999	St. Charles	
	116	US- 6,053,176	4/25/2000	Adams et al.	
	118	US- 6,095,153	8/1/2000	Kessler et al.	
	119	US- 6,102,036	8/15/2000	Slutsky et al.	
	120	US- 6,125,853	10/3/2000	Susa et al.	
	121	US- 6,155,268	12/5/2000	Takeuchi	
	122	US- 6,164,287	12/26/2000	White	
	123	US- 6,234,169	5/22/2001	Bulbrook et al.	
	124	US- 6,269,966	8/7/2001	Pallo et al.	
	125	US- 6,349,728	2/26/2002	Pham	
	126	US- 6,381,739	4/30/2002	Breternitz Jr. et al.	
	127	US- 6,386,371	5/14/2002	Parsons	
	128	US- 6,431,363	8/13/2002	Hacker	
	129	US- 6,446,793	9/10/2002	Layshock	
	130	US- 6,510,982	1/28/2003	White et al.	
	131	US- 6,532,965	3/18/2003	Abhulimen et al.	
	132	US- 6,536,442	3/25/2003	St. Charles et al.	
	133	US- 6,557,708	5/6/2003	Polacco	
	134	US- 6,598,607	7/29/2003	Adiga et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	413	WO03/082031A1	10/9/2003	Steinberg, Dan A.		
	414	WO03/094900A1	11/20/2003	Alexza Molecular Delivery		
	415	WO2004/064548A1	8/5/2004	Netzer, Omry		
	417	WO2005/020726A1	3/10/2005	Lee, Seunghyun		
	418	WO2006/015070A1	2/9/2006	Brown & Williamson Tob.		
	419	WO2007/026131A1	3/8/2007	Acetate Products Ltd		

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 8 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	135	US- 6,606,998	8/19/2003	Gold	
	136	US- 6,615,840	9/9/2003	Fournier et al.	
	137	US- 6,622,867	9/23/2003	Menceles	
	138	US- 6,655,379	12/2/2003	Clark et al.	
	139	US- 6,672,762	1/6/2004	Faircloth et al.	
	140	US- 6,688,313	2/10/2004	Wrenn et al.	
	141	US- 6,726,006	4/27/2004	Funderburk et al.	
	142	US- 6,772,756	8/10/2004	Shayan	
	143	US- 6,799,576	10/5/2004	Farr	
	144	US- 6,803,545	10/12/2004	Blake et al.	
	145	US- 6,805,545	10/19/2004	Slaboden	
	146	US- 6,810,883	11/2/2004	Felter et al.	
	147	US- 6,827,573	12/7/2004	St. Charles et al.	
	148	US- 6,954,979	10/18/2005	Logan	
	149	US- 7,000,775	2/21/2006	Gelardi et al.	
	151	US- 7,488,171	2/10/2009	St. Charles et al.	
	152	US- 7,546,703	6/16/2009	Johnske et al.	
	153	US- 7,621,403	11/24/2009	Althoff et al.	
	154	US- 7,644,823	1/12/2010	Gelardi et al.	

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)			
	421	WO2010/023561A1	3/4/2010	Actavis Group Ptc	
	422	WO2011/033396A2	3/24/2011	Minilogic Device Corp Ltd	
	423	WO2011/117580A2	9/29/2011	Kind Consumer Ltd	
	424	WO2012/021972A1	2/23/2012	Cogestor Inc.	
	425	WO2012/027350A2	3/1/2012	Alelov, Eli	
	426	WO2012/085207A1	6/28/2012	Philip Morris Prod S.A	

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 9 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	155	US- 7,767,698	8/3/2010	Warchol et al.	
	156	US- 7,815,332	10/19/2010	Smith	
	157	US- 7,832,410	11/16/2010	Hon	
	158	US- 7,886,507	2/15/2011	McGuinness Jr.	
	159	US- 7,988,034	8/2/2011	Pezzoli	
	160	US- 8,141,701	3/27/2012	Hodges	
	161	US- 8,156,944	4/17/2012	Hon	
	162	US- 8,322,350	12/4/2012	Lipowicz	
	163	US- 8,371,310	2/12/2013	Brenneise	
	164	US- 8,381,739	2/26/2013	Gonda	
	165	US- 8,387,612	3/5/2013	Damani et al.	
	166	US- 8,443,534	5/21/2013	Goodfellow et al.	
	167	US- 8,490,629	7/23/2013	Shenassa et al.	
	168	US- 8,539,959	9/24/2013	Scatterday	
	169	US- 8,541,401	9/24/2013	Mishra et al.	
	170	US- 8,596,460	12/3/2013	Scatterday	
	171	US- 8,671,952	3/18/2014	Winterson et al.	
	172	US- 8,741,348	6/3/2014	Hansson et al.	
	175	US- 8,915,254	12/23/2014	Monsees et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	428	WO2013/050934A1	4/11/2013	SIS Resources Ltd.		
	429	WO2013/083635A1	6/13/2013	Philip Morris Prod S.A		
	431	WO2013/098398A2	7/4/2013	Philip Morris Prod S.A		
	432	WO2013/142678A1	9/26/2013	Njoy Inc.		
	434	WO2014/093127A2	6/19/2014	Fuisz, Richard C.		
	436	WO2014/118286A2	8/7/2014	Philip Morris Prod S.A		

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 10

of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	176	US- 8,925,555	1/6/2015	Monsees et al.	
	354	US- 2015/0157056**	6/11/2015	Bowen et al.	
	179	US- 9,215,895**	12/22/2015	Bowen et al.	
	180	US- D590990	4/21/2009	Hon	
	181	US- D590991	4/21/2009	Hon	
	182	US- D624238	9/21/2010	Turner	
	183	US- D642330	7/26/2011	Turner	
	184	US- D644375	8/30/2011	Zhou	
	185	US- D653803	2/7/2012	Timmermans	
	186	US- D691324	10/8/2013	Saliman	
	187	US- D695450	12/10/2013	Benassayag et al.	
	188	US- D707389	6/17/2014	Liu	
	189	US- 2001/0015209	8/23/2001	Zielke	
	190	US- 2001/0032643	10/25/2001	Hochrainer et al.	
	191	US- 2001/0032795	10/25/2001	Weinstein et al.	
	192	US- 2001/0052480	12/20/2001	Kawaguchi et al.	
	193	US- 2002/0078951	6/27/2002	Nichols et al.	
	194	US- 2002/0175164	11/28/2002	Dees et al.	
	195	US- 2003/0005926	1/9/2003	Jones et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	437	WO2014/139611A1	9/18/2014	Philip Morris Prod S.A		
	438	WO2014/140087A1	9/18/2014	Philip Morris Prod S.A		
	440	WO2014/187763A1	11/27/2014	Philip Morris Prod S.A		
	441	WO2014/187770A2	11/27/2014	Philip Morris Prod S.A		
	443	WO2015/006652A1	1/15/2015	Alexza Pharm. Inc.		
	445	WO2015/040180A2	3/26/2015	Philip Morris Prod S.A		

Examiner
Signature

/Dionne Walls Mayes/

Date

Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 11 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	360	US- 2015/0208729**	7/30/2015	Monsees et al.	
	196	US- 2003/0089377	5/15/2003	Hajaligol et al.	
	197	US- 2004/0031495	2/19/2004	Steinberg	
	198	US- 2004/0099266	5/27/2004	Cross et al.	
	199	US- 2004/0149296	8/5/2004	Rostami et al.	
	200	US- 2004/0149624	8/5/2004	Wischusen et al.	
	201	US- 2004/0173229	9/9/2004	Crooks et al.	
	202	US- 2004/0182403	9/23/2004	Andersson et al.	
	203	US- 2004/0221857	11/11/2004	Dominguez	
	204	US- 2004/0237974	12/2/2004	Min	
	205	US- 2005/0016549	1/27/2005	Banerjee et al.	
	206	US- 2005/0016550	1/27/2005	Katase	
	207	US- 2005/0034723	2/17/2005	Bennett et al.	
	208	US- 2005/0061759	3/24/2005	Doucette	
	209	US- 2005/0118545	6/2/2005	Wong	
	210	US- 2005/0145533	7/7/2005	Seligson	
	211	US- 2005/0172976	8/11/2005	Newman et al.	
	212	US- 2005/0244521	11/3/2005	Strickland et al.	
	213	US- 2005/0268911	12/8/2005	Cross et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	448	WO2015/082652A1	6/11/2015	Philip Morris Prod S.A		
	449	WO2015/084544A1	6/11/2015	Pax Labs, Inc.		
	451	WO2015/101651A1	7/9/2015	Philip Morris Prod S.A		
	453	WO2015/124878A1(EngAbs)	8/27/2015	Smokio		
	454	WO2015/148547A1	10/1/2015	Nicotech LLC		
	455	WO2015/175979A1	11/19/2015	Pax Labs, Inc.		

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 12 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	214	US- 2006/0018840	1/26/2006	Lechuga Ballesteros et al.	
	215	US- 2006/0054676	3/16/2006	Wischusen	
	216	US- 2006/0102175	5/18/2006	Nelson	
	217	US- 2006/0150991	7/13/2006	Lee	
	218	US- 2006/0191546	8/31/2006	Takano et al.	
	219	US- 2006/0191548	8/31/2006	Strickland et al.	
	371	US- 2015/0313285	11/5/2015	Waller et al.	
	221	US- 2006/0254948	11/16/2006	Herbert et al.	
	222	US- 2006/0255105	11/16/2006	Sweet	
	223	US- 2007/0006889	1/11/2007	Kobal et al.	
	224	US- 2007/0045288	3/1/2007	Nelson	
	225	US- 2007/0062548	3/22/2007	Horstmann et al.	
	226	US- 2007/0074734	4/5/2007	Braunshteyn et al.	
	227	US- 2007/0098148	5/3/2007	Sherman	
	228	US- 2007/0102013	5/10/2007	Adams et al.	
	229	US- 2007/0144514	6/28/2007	Yeates et al.	
	230	US- 2007/0163610	7/19/2007	Lindell et al.	
	231	US- 2007/0215164	9/20/2007	Mehio	
	232	US- 2007/0235046	10/11/2007	Gedevanishvili	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

Examiner
Signature

/Dionne Walls Mayes/

Date

Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**
TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 13

of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	233	US- 2007/0267033	11/22/2007	Mishra et al.	
	234	US- 2007/0280652	12/6/2007	Williams	
	235	US- 2007/0283972**	12/13/2007	Monsees et al.	
	236	US- 2008/0023003	1/31/2008	Rosenthal	
	237	US- 2008/0029095	2/7/2008	Esser	
	238	US- 2008/0092912	4/24/2008	Robinson et al.	
	239	US- 2008/0149118	6/26/2008	Oglesby et al.	
	240	US- 2008/0216828	9/11/2008	Wensley et al.	
	241	US- 2008/0241255	10/2/2008	Rose et al.	
	242	US- 2008/0257367	10/23/2008	Paterno et al.	
	243	US- 2008/0276947	11/13/2008	Martzel	
	244	US- 2009/0004249	1/1/2009	Gonda	
	245	US- 2009/0095287	4/16/2009	Emarlou	
	246	US- 2009/0126745	5/21/2009	Hon	
	247	US- 2009/0133691	5/28/2009	Yamada et al.	
	248	US- 2009/0230117	9/17/2009	Fernando et al.	
	249	US- 2009/0255534	10/15/2009	Paterno	
	250	US- 2009/0267252	10/29/2009	Ikeyama	
	251	US- 2009/0272379	11/5/2009	Thorens et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 14

of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	252	US- 2009/0288668	11/26/2009	Inagaki	
	253	US- 2009/0288669	11/26/2009	Hutchens	
	254	US- 2009/0293892	12/3/2009	Williams et al.	
	255	US- 2009/0293895	12/3/2009	Axelsson et al.	
	256	US- 2010/0000672	1/7/2010	Fogle	
	257	US- 2010/0006092	1/14/2010	Hale et al.	
	258	US- 2010/0024834	2/4/2010	Oglesby et al.	
	259	US- 2010/0031968	2/11/2010	Sheikh et al.	
	260	US- 2010/0156193	6/24/2010	Rhodes et al.	
	261	US- 2010/0163063	7/1/2010	Fernando et al.	
	262	US- 2010/0186757	7/29/2010	Crooks et al.	
	264	US- 2010/0236562	9/23/2010	Hearn et al.	
	265	US- 2010/0242974	9/30/2010	Pan	
	266	US- 2010/0242976	9/30/2010	Katayama et al.	
	267	US- 2010/0275938	11/4/2010	Roth et al.	
	268	US- 2010/0276333	11/4/2010	Couture	
	269	US- 2010/0307116	12/9/2010	Fisher	
	270	US- 2011/0030706	2/10/2011	Gibson et al.	
	271	US- 2011/0036346	2/17/2011	Cohen et al.	

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)			

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 15 of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	272	US- 2011/0041861	2/24/2011	Sebastian et al.	
	273	US- 2011/0049226	3/3/2011	Moreau et al.	
	274	US- 2011/0094523	4/28/2011	Thorens et al.	
	275	US- 2011/0108023	5/12/2011	McKinney et al.	
	276	US- 2011/0155153	6/30/2011	Thorens et al.	
	277	US- 2011/0162667	7/7/2011	Burke et al.	
	278	US- 2011/0180433	7/28/2011	Rennecamp	
	279	US- 2011/0192397	8/11/2011	Saskar et al.	
	280	US- 2011/0226236	9/22/2011	Buchberger	
	281	US- 2011/0226266	9/22/2011	Tao	
	282	US- 2011/0232654	9/29/2011	Mass	
	283	US- 2011/0236002	9/29/2011	Oglesby et al.	
	284	US- 2011/0265806	11/3/2011	Alarcon et al.	
	285	US- 2011/0268809	11/3/2011	Brinkley et al.	
	286	US- 2011/0277780	11/17/2011	Terry et al.	
	287	US- 2011/0278189	11/17/2011	Terry et al.	
	288	US- 2011/0315701	12/29/2011	Everson	
	289	US- 2012/0006342	1/12/2012	Rose et al.	
	290	US- 2012/0111347	5/10/2012	Hon	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08A (04-07)

Approved for use through 09/30/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 16 of 20

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	291	US- 2012/0199146	8/9/2012	Marangos	
	292	US- 2012/0204889	8/16/2012	Xiu	
	293	US- 2012/0227753	9/13/2012	Newton	
	294	US- 2012/0255567	10/11/2012	Rose et al.	
	295	US- 2012/0260927	10/18/2012	Liu	
	296	US- 2012/0267383	10/25/2012	Van Rooyen	
	298	US- 2012/0325227	12/27/2012	Robinson et al.	
	299	US- 2013/0042865**	2/21/2013	Monsees et al.	
	300	US- 2013/0068239	3/21/2013	Youn	
	301	US- 2013/0140200	6/6/2013	Scatterday	
	302	US- 2013/0152922	6/20/2013	Benassayag et al.	
	303	US- 2013/0186416	7/25/2013	Gao et al.	
	304	US- 2013/0228191	9/5/2013	Newton	
	305	US- 2013/0247924	9/26/2013	Scatterday et al.	
	306	US- 2013/0248385	9/26/2013	Scatterday et al.	
	307	US- 2013/0255702	10/3/2013	Griffith Jr. et al.	
	308	US- 2013/0276802	10/24/2013	Scatterday	
	309	US- 2013/0312742**	11/28/2013	Monsees et al.	
	311	US- 2013/0333700	12/19/2013	Buchberger	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

Examiner
Signature

/Dionne Walls Mayes/

Date
Considered

03/31/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 17

of 20

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	315	US- 2014/0041655	2/13/2014	Barron et al.	
	317	US- 2014/0060552**	3/6/2014	Cohen	
	325	US- 2014/0190503	7/10/2014	Li et al.	
	326	US- 2014/0196731	7/17/2014	Scatterday	
	372	US- 2016/0044967**	2/18/2016	Bowen et al.	
	334	US- 2014/0345631**	11/27/2014	Bowen et al.	
	335	US- 2014/0345635	11/27/2014	Rabinowitz et al.	
	337	US- 2014/0366898**	12/18/2014	Monsees et al.	
	338	US- 2014/0378790**	12/25/2014	Cohen	
	339	US- 2015/0020823	1/22/2015	Lipowicz et al.	
	342	US- 2015/0027468	1/29/2015	Li et al.	
	350	US- 2015/0128966	5/14/2015	Lord	
	353	US- 2015/0150308**	6/4/2015	Monsees et al.	
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)			

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08b (07-09)

Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known			
		Application Number	14/925,968		
		Filing Date	October 28, 2015		
		First Named Inventor	Adam Bowen		
		Art Unit	1747		
		Examiner Name	Mayes, Dionne Walls		
Sheet	18	of	20	Attorney Docket Number	13211-713.303

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	456	ECF; Any interest in determining nicotine--by DVAP; (https://www.e-cigarette-forum.com/forum/threads/any-interest-in-determining-nicotine-by-dvap.35922/); blog posts dated: 2009; 8 pgs.; print/retrieval date: July 31, 2014	
	457	BOMBICK et al.; Chemical and biological studies of a new cigarette that primarily heats tobacco; Part 2: In vitro toxicology of mainstream smoke condensate; Food and Chemical Toxicology; 36(3); pp. 183-190; March 1998	
	458	BOMBICK et al.; Chemical and biological studies of a new cigarette that primarily heats tobacco; Part 3: In vitro toxicity of whole smoke; Food and Chemical Toxicology; 36(3); pp. 191-197; March 1998	
	459	BORGERDING et al.; Chemical and biological studies of a new cigarette that primarily heats tobacco; Part 1: Chemical composition of mainstream smoke; Food and Chemical Toxicology; 36(3); pp. 169-182; March 1998	
	460	MIRRIAM-WEBSTER Online Dictionary; Lighter; retrieved 1/4/2013 from the internet: (http://www.merriam-webster.com/dictionary/lighter?show=0&t=1357320593); 2 pgs.; print date: 1/4/2013	
	461	BAKER et al.; The pyrolysis of tobacco ingredients; J. Anal. Appl. Pyrolysis; 71(1); pp. 223-311; March 2004	
	462	TORIKAI et al.; Effects of temperature, atmosphere and pH on the generation of smoke compounds during tobacco pyrolysis; Food and Chemical Toxicology; 42(9); pp. 1409-1417; September 2004	
	463	WARD; Green leaf threshing and redrying tobacco; Section 10B; in TOBACCO Production, Chemistry and Technology; Davis and Nielsen (Eds.); Blackwell Science Ltd.; pp. 330-333; July 15, 1999	
	464	INGEBRETHSEN et al.; Electronic cigarette aerosol particle size distribution measurements; Inhalation Toxicology; 24(14); pp. 976-984; December 2012	
	465	McCANN et al.; Detection of carcinogens as mutagens in the salmonella/microsome test: Assay of 300 chemicals: Discussion; Proc. Nat. Acad. Sci.; 73(3); pp. 950-954; March 1976	

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.
ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08b (07-09)

Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	14/925,968
		Filing Date	October 28, 2015
		First Named Inventor	Adam Bowen
		Art Unit	1747
Examiner Name	Mayes, Dionne Walls		
Sheet 19 of 20	Attorney Docket Number		13211-713.303

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	466	WELLS; Glycerin as a constituent of cosmetics and toilet preparations; Journal of the Society of Cosmetic Chemists; 9(1); pp. 19-25; January 1958	
	467	KUO et al.; Appendix D: Particle size-U.S. sieve size and tyler screen mesh equivalents; Applications of Turbulent and Multiphase Combustion; John Wiley & Sons, Inc.; pp. 541-543; May 1, 2012	
	468	HARVEST VAPOR; American Blend Tobacco (product info.); retrieved from the internet (http://harvestvapor.com/); 2 pgs.; print/retrieval date: 10/10/2014	
	469	INCHEM; Levulinic Acid; JECFA Evaluation Summary; retrieved 10/10/2014 from http://www.inchem.org/documents/jecfa/feceval/jec_1266.htm ; 1 pg.; March 10, 2003	
	470	INCHEM; Benzoic Acid; JECFA Evaluation Summary; retrieved 10/10/2014 from http://www.inchem.org/documents/jecfa/feceval/jec_184.htm ; 2 pgs.; May 28, 2005	
	471	FOOD & DRUG ADMINISTRATION; Warning letter to The Compounding Pharmacy; retrieved 10/10/2014 from http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2002/ucm144843.htm ; 3 pgs.; April 9, 2002	
	472	INCHEM; Pyruvic Acid; JECFA Evaluation Summary; retrieved 10/10/2014 from http://www.inchem.org/documents/jecfa/feceval/jec_2072.htm ; 1 pg.; January 29, 2003	
	473	INCHEM; Sorbic Acid; JECFA Evaluation Summary; retrieved 10/10/2014 from http://www.inchem.org/documents/jecfa/feceval/jec_2181.htm ; 1 pg.; May 29, 2005	
	474	FLOURIS et al.; Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function; Inhal. Toxicol.; 25(2); pp. 91-101; Feb 2013	
	475	GONIEWICZ et al.; Nicotine levels in electronic cigarettes; Nicotine Tobacco Research; 15(1); pp. 158-166; Jan 2013	

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.
ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

PTO/SB/08b (07-09)

Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	14/925,968
				Filing Date	October 28, 2015
				First Named Inventor	Adam Bowen
				Art Unit	1747
				Examiner Name	Mayes, Dionne Walls
Sheet	20	of	20	Attorney Docket Number	13211-713.303

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	476	SEEMAN et al.; The form of nicotine in tobacco. Thermal transfer of nicotine and nicotine acid salts to nicotine in the gas phase; J Aric Food Chem.; 47(12); pp. 5133-5145; Dec 1999	
	477	VANSICKEL et al.; A clinical laboratory model for evaluating the acute effects of electronic cigarettes: Nicotine delivery profile and cardiovascular and subjective effects; Cancer Epidemiology Biomarkers Prevention; 19(8); pp. 1945-1953; (online) July 20, 2010	
	478	ZHANG et al.; In vitro particle size distributions in electronic and conventional cigarette aerosols suggest comparable deposition patterns; Nicotine Tobacco Research; 15(2); pp. 501-508; Feb 2013	
	479	NICOLI et al.; Mammalian tumor xenografts induce neovascularization in Zebrafish embryos; Cancer Research; 67(7); pp. 2927-2931; April 1, 2007	
	480	YouTube; Firefly Vaporizer Review w/ Usage Tips by The Vape Critic; retrieved from the internet (http://www.youtube.com/watch?v=1J38N0AV7wI); 1 pg.; published 12/10/2013; download/print date: 2/18/2015	
	483	PERFETTI; Structural study of nicotine salts; Beitrage zur Tabakforschung International; Contributions to Tobacco Research; 12(2); pp. 43-54; June 1983	
	484	MONSEES, J.; U.S. Pat. App. # 12/115,400 entitled "Method And System For Vaporization Of A Substance", filed 5/5/2008	
	485	BOWEN et al.; U.S. Pat. App. # 14/960,259 entitled "Calibrated Dose Control", filed 12/4/2015	

Examiner Signature	/Dionne Walls Mayes/	Date Considered	03/31/2016
--------------------	----------------------	-----------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.
ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<p>Substitute for form 1449/PTO</p> <p style="text-align: center; font-weight: bold; font-size: 1.2em;">INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p style="text-align: center; font-style: italic;">(Use as many sheets as necessary)</p>	<p style="text-align: center; font-weight: bold; font-size: 1.2em;">Complete if Known</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Application Number</td> <td>14/925,968</td> </tr> <tr> <td>Filing Date</td> <td>October 28, 2015</td> </tr> <tr> <td>First Named Inventor</td> <td>Adam Bowen</td> </tr> <tr> <td>Art Unit</td> <td>1747</td> </tr> <tr> <td>Examiner Name</td> <td>Mayes, Dionne Walls</td> </tr> <tr> <td>Attorney Docket Number</td> <td>13211-713.303</td> </tr> </table>	Application Number	14/925,968	Filing Date	October 28, 2015	First Named Inventor	Adam Bowen	Art Unit	1747	Examiner Name	Mayes, Dionne Walls	Attorney Docket Number	13211-713.303
Application Number	14/925,968												
Filing Date	October 28, 2015												
First Named Inventor	Adam Bowen												
Art Unit	1747												
Examiner Name	Mayes, Dionne Walls												
Attorney Docket Number	13211-713.303												

[illegible][illegible]

Examiner Signature	/Dionne Walls Mayes/	Date Considered	04/27/2016
-----------------------	----------------------	--------------------	------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /D.W.M./

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	389	nicotine near50 (lactic or lactate)	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/27 09:16
L2	440	nicotine near50 (lactic or lactate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/04/27 09:16
L3	65	((a24f47/00)".cpc" or (131/\$.ccls.) or (128/\$).ccls.) and nicotine near50 (lactic or lactate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/04/27 09:20
L4	70	((a24f47/00).cpc. or (131/\$.ccls.) or (128/\$).ccls.) and nicotine near50 (lactic or lactate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/04/27 09:20
L5	73	((a24f47/00 or a24f47/008).cpc. or (131/\$.ccls.) or (128/\$).ccls.) and nicotine near50 (lactic or lactate)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/04/27 09:20
L8	1	("9,215,895").PN.	US-PGPUB; USPAT	OR	OFF	2016/04/27 11:18
L9	6717	(a24f47/00 or a24f47/008).cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2016/04/27 18:29
S1	3	((("20060195518") or ("20120256567") or ("20080241255")).PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 11:41
S2	3	((("20060195518") or ("20120255567") or ("20080241255")).PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 11:41
S3	2	((("20120255567") or ("20080241255")).PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 11:42
S4	0	("2006").pn. and (hon).in.	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 11:42

S5	42	(hon).in. and cigarette	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 11:44
S6	25	("131"/\$ or "128"/\$).ccls. and electronic cigarette and nicotine and plasma	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:06
S7	6	("131"/\$ or "128"/\$).ccls. and (fuisz).in. and nicotine and plasma	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:06
S8	91	("131"/\$ or "128"/\$).ccls. and inhal\$5 near15 nicotine and plasma	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:15
S9	25	("131"/\$ or "128"/\$).ccls. and inhal\$5 near15 nicotine and plasma and ((max or maxim\$3) near25 time)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:16
S10	23	("131"/\$ or "128"/\$).ccls. and inhal\$5 near15 nicotine and (plasma near25 (peak or max or maxim\$3) near25 time)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:25
S11	9	("131"/\$ or "128"/\$).ccls. and inhal\$5 same (nicotine same (plasma near25 (peak or max or maxim\$3) near25 time))	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 15:25
S12	9	("131"/\$ or "128"/\$).ccls. and inhal\$5 same (nicotine same (plasma near25 (peak or max or maxim\$3) near25 time))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 15:26
S13	32	("131"/\$ or "128"/\$).ccls. and inhal\$5 and (nicotine same (plasma near25 (peak or max or maxim\$3) same time))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 15:28
S14	2	("131"/\$ or "128"/\$).ccls. and nicotine benzoate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 15:51
S15	2	(vaporiz\$3 or electronic cigarette) and nicotine benzoate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 15:52
S16	346	("131"/\$ or "128"/\$).ccls. and (salt near5 nicotine)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 15:53
S17	230	("131"/\$ or "128"/\$).ccls. and (salt near5 nicotine) same (acid)	US-PGPUB; USPAT; USOCR; FPRS;	ADJ	ON	2015/01/20 15:54

			EPO; JPO; DERWENT IBM_TDB			
S18	210	("131"/\$ or "128"/\$).ccls. and (salt near5 nicotine) near35 (acid)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 15:55
S19	17	("131"/\$ or "128"/\$).ccls. and (salt near5 nicotine) near35 (carboxylic or citric)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 16:08
S20	1	("2356185").PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 16:32
S21	1	("2356185").PN.	USOCR	OR	OFF	2015/01/20 16:33
S22	4	nicotine benzoate	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 16:38
S23	1	("20010029959").PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 16:43
S24	0	electronic cigarette and inhal\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 16:47
S25	1	nicotine and inhal\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/01/20 16:48
S26	1	nicotine and inhal\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 16:59
S27	53	inhal\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 17:33
S28	222	puff\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT IBM_TDB	ADJ	ON	2015/01/20 17:37
S29	207	("131"/\$ or "128"/\$ or cigarette) and puff\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR;	ADJ	ON	2015/01/20 17:40

			FPRS; EPO; JPO; DERWENT; IBM_TDB			
S30	179	("131"/\$ or "128"/\$) and puff\$4 near25 every near15 (seconds or secs)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT; IBM_TDB	ADJ	ON	2015/01/20 17:40
S31	28	((("20070163610") or ("20090293895") or ("20130186416") or ("7832410") or ("8,156,944") or ("8,511,318") or ("20140345631") or ("20140345635") or ("20040191322") or ("20060018840") or ("20060196518") or ("20080241255") or ("20090004249") or ("20100242976") or ("20110268809") or ("20120255567") or ("4,830,028") or ("4,836,224") or ("6,102,036") or ("6,234,169") or ("6,799,576") or ("6,874,507") or ("7,767,698") or ("8,079,371") or ("8,322,350") or ("8,375,957") or ("8,381,739") or ("8,741,348"))).PN.	US-PGPUB; USPAT	OR	OFF	2015/01/20 20:10
S32	1	(14/512311).APP.	US-PGPUB; USPAT	OR	OFF	2015/03/23 22:03
S33	1	(14/512311).APP.	US-PGPUB; USPAT	OR	OFF	2015/05/14 15:25
S34	1605	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:07
S35	237	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:08
S36	221	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5 or mouth or oral\$4)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:08
S37	191	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5 or mouth or oral\$4) and (plasma or blood)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:08
S38	163	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5 or mouth or oral\$4) and (plasma or blood) and ph	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:09
S39	108	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5 or mouth or oral\$4) and (plasma or blood) and ph and ((drop\$4 or vapor\$4 or aerosol\$4 or particle) near25 size)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:10
S40	87	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5 or mouth or oral\$4) and (plasma or blood) and ph and ((drop\$4 or vapor\$4 or	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:11

		aerosol\$4 or particle) near25 size) and heat\$4				
S41	77	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5) and (plasma or blood) and ph and ((drop\$4 or vapor\$4 or aerosol\$4 or particle) near25 size) and heat\$4	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 16:12
S42	4	("2004076289").PN.	FPRS; EPO; JPO	OR	OFF	2015/05/14 18:13
S43	15	ANDERSSON near3 SVEN-BORJE	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:15
S44	13	ANDERSSON near3 SVEN-BORJE and nicotine	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:15
S45	71	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5) and (plasma or blood) and ph and ((drop\$4 or vapor\$4 or aerosol\$4 or particle) near25 size) and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:26
S46	21	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5) and (plasma or blood) and (ph near5 "7") and ((drop\$4 or vapor\$4 or aerosol\$4 or particle) near25 size) and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:27
S47	26	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5) and (plasma or blood) and (ph near5 "7") and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:28
S48	38	("128"/\$ or "131"/\$ or "424"/\$ or "514"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and benzoic and (inhal\$5) and (plasma or blood) and (ph near5 "7") and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/14 18:31
S49	1	("20060196518").PN.	US-PGPUB; USPAT	OR	OFF	2015/05/14 19:32
S50	34	("128"/\$ or "131"/\$ or "424"/\$ or "514"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and (salicylic or sorbic or lauric or levulinic or citric or benzoic or pyruvic) and (inhal\$5) and ((plasma or blood or peek or peak) near10 concentration) and (ph near5 "7") and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/15 08:30
S51	1	("8831739").PN.	US-PGPUB; USPAT	OR	OFF	2015/05/15 08:43
S52	1	("8381739").PN.	US-PGPUB; USPAT	OR	OFF	2015/05/15 08:43
S53	14	(igor near3 gonda) and nicotine and ng/ml	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/15 10:42
S54	13	(igor near3 gonda) and nicotine near50	US-PGPUB;	ADJ	ON	2015/05/15

		concentration near50 ng/ml	USPAT; USOCR			10:42
S55	0	(igor near3 gonda) and nicotine near50 concentration near50 ng/ml near50 salt	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/15 10:43
S56	64	(igor near3 gonda) and ((blood or plasma or nicotine) near50 concentration)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/15 10:46
S57	13	(igor near3 gonda) and ((blood or plasma or nicotine) near50 concentration) same nicotine	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/05/15 10:46
S58	1	("20030136404").PN.	US-PGPUB; USPAT	OR	OFF	2015/05/17 15:16
S59	1	(14/512311).APP.	US-PGPUB; USPAT	OR	OFF	2015/07/14 09:12
S60	1	("20140261474").PN.	US-PGPUB; USPAT	OR	OFF	2015/07/14 10:27
S61	1	(14/512311).APP.	US-PGPUB; USPAT	OR	OFF	2015/09/17 14:40
S62	934	(A24F47/008).cpc.	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/09/17 14:46
S63	78	("128"/\$ or "131"/\$ or "424"/\$ or "514"/\$.ccls. and nicotine near25 (formulation or solution or liquid or solvent) and acid and (inhal\$5) and (plasma or blood) and (ph near5 "7") and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/09/17 14:46
S64	367	("128"/\$ or "131"/\$ or "424"/\$ or "514"/\$.ccls. and nicotine near25 (formulation or solution or liquid or solvent) and acid and (inhal\$5) and (plasma or blood) and heat\$4 and lung	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/09/17 14:47
S65	283	("128"/\$ or "131"/\$ or "424"/\$.ccls. and nicotine near25 (formulation or solution or liquid or solvent) and (levulinic or pyruvic or salicylic or sorbic or lauric or benzoic) and (inhal\$5 or mouth or oral\$4) and (plasma or blood)	US-PGPUB; USPAT; USOCR	ADJ	ON	2015/09/17 14:48
S69	2	((("20060196518") or ("20140261474"))).PN.	US-PGPUB; USPAT	OR	OFF	2015/12/10 16:09
S70	1	("9215895").PN.	US-PGPUB; USPAT	OR	OFF	2016/03/30 20:38
S71	0	(14/925958).APP.	US-PGPUB; USPAT	OR	OFF	2016/04/24 10:41
S72	1	(14/925968).APP.	US-PGPUB; USPAT	OR	OFF	2016/04/24 10:41
S73	2	(12/236439).APP.	US-PGPUB; USPAT	OR	OFF	2016/04/24 10:56
S74	120	(A24F47/008).cpc. and temperature near25 ("100" or "200" or "300")	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 12:53
S75	34	(A24F47/008).cpc. and temperature near25 ("100" or "200" or "300") near25 degrees	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 12:56
S76	35	(A24F47/008 or A24F47/00 or A24F47/002).cpc. and temperature near25	US-PGPUB; USPAT;	ADJ	ON	2016/04/25 12:57

		("100" or "200" or "300") near25 degrees	USOCR			
S77	0	((128/\$ or 131/\$).ccls. or (A24F47/008 or A24F47/00 or A24F47/002).cpc.) and low temperature and ("100" or "200" or "300") near25 degrees	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 13:27
S78	1787	((128/\$ or 131/\$).ccls. or (A24F47/008 or A24F47/00 or A24F47/002).cpc.) and low temperature	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 13:28
S79	118	((128/\$ or 131/\$).ccls. or (A24F47/008 or A24F47/00 or A24F47/002).cpc.) and low temperature and ("100" or "200" or "300") near25 degrees	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 13:28
S80	29	((128/\$ or 131/\$).ccls. or (A24F47/008 or A24F47/00 or A24F47/002).cpc.) and low temperature and ("100" or "200" or "300") near25 degrees and nicotine	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 13:29
S81	2	(12/336439).APP.	US-PGPUB; USPAT	OR	OFF	2016/04/25 13:38
S82	1	("5,544,646").PN.	US-PGPUB; USPAT	OR	OFF	2016/04/25 19:16
S83	10	(rose).in. and pyruvic and nicotine	US-PGPUB; USPAT; USOCR	ADJ	ON	2016/04/25 19:18
S84	1	(12/481908).APP.	US-PGPUB; USPAT	OR	OFF	2016/04/25 21:20

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S66	723	(A24F47/008).cpc.	US-PGPUB	ADJ	ON	2015/09/17 14:46
S67	246	("128"/\$ or "131"/\$ or "424"/\$ or "514"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and acid and (inhal\$5) and (plasma or blood) and heat\$4 and lung	US-PGPUB	ADJ	ON	2015/09/17 14:47
S68	196	("128"/\$ or "131"/\$ or "424"/\$).ccls. and nicotine near25 (formulation or solution or liquid or solvent) and (levulinic or pyruvic or salicylic or sorbic or lauric or benzoic) and (inhal\$5 or mouth or oral\$4) and (plasma or blood)	US-PGPUB	ADJ	ON	2015/09/17 14:49

4/ 27/ 2016 6:29:31 PM**C:\Users\dmayes\Documents\EAST\Workspaces\14925968.wsp**

FAX COVER SHEET

FAX No: 571-273-5836
ATTN: Examiner Mayes (Dionne Walls Mayes)
Date: June 8, 2016

Number of pages (including cover sheet): 3

RE: Telephone interview on Thursday, June 9, 2016 for App. no. 14/925,968

From: Rick Shoop
Return Fax: 1-650-212-7562
Direct Dial: 1-650-283-2092 (cell)

NOTES

See attached

June 8, 2016

RE: Telephone interview on Thursday, June 9, 2016 at 10 am PT (1pm ET) for App. no. 14/925,968

Dear Examiner Mayes:

Thank you for making time to talk about this application; I'm looking forward to talking with you tomorrow at 1pm ET (10 am PT). I'll give you a call then. During the call I'd like to discuss the new principle reference (Griffith) and the combination with Gonda. For our discussion, I'm attaching some claim amendment language.

Please let me know if there are any changes in your schedule, or if you need anything ahead of the call. Thanks again!

Best,
Rick Shoop



FOR DISCUSSION ONLY
--- DO NOT ENTER ---

1. (POSSIBLE AMENDMENTS - DO NOT ENTER) A method of delivering nicotine to a user comprising:

deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier, wherein:

- a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
- b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and
- c. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from a fluid storage reservoir to an atomizer and heating at least a portion of the nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C;

wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.

7. (POSSIBLE AMENDMENTS - DO NOT ENTER) A method of delivering nicotine to a user comprising:

deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage reservoir connected to a heating element by a wick, wherein:

- a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
- b. the nicotine formulation comprises protonated nicotine;
- c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol;

- d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the low-temperature vaporizer; and
 - e. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from the fluid storage reservoir to the heating element and heating at least a portion of the nicotine formulation between about 100°C and 300°C to generate an inhalable aerosol;
- wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P. O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/925,968	10/28/2015	Adam BOWEN	13211-713.303	2707
66854	7590	06/14/2016		
SHAY GLENN LLP 2755 CAMPUS DRIVE SUITE 210 SAN MATEO, CA 94403			EXAMINER MAYES, DIONNE WALLS	
			ART UNIT	PAPER NUMBER
			1747	
			NOTIFICATION DATE	DELIVERY MODE
			06/14/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@shayglenn.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 14/925,968	Applicant(s) BOWEN ET AL.	
	Examiner DIONNE W. MAYES	Art Unit 1747	

All participants (applicant, applicant's representative, PTO personnel):

(1) DIONNE W. MAYES. (3) _____.

(2) RICHARD SHOOP. (4) _____.

Date of Interview: 09 June 2016.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☒Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: Those of Record.

Identification of prior art discussed: Griffith, Jr. et al (20130255702) and Gonda (2014/0261474).

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicant's representative, Mr. Richard Shoop, proposed claim amendments, to the independent claims, which include recitation related to "wicking" of the nicotine formulation from a fluid reservoir to an atomizer/heating element. Examiner Mayes indicated that, after a cursory look of the primary reference, Griffith, Jr. et al, this "wicking" feature/structure did not appear to be apparent and further consideration would need to be taken to determine whether modifying the Griffith, Jr reference to include this feature would even be obvious. The Examiner also indicated that an updated search would need to be conducted. Lastly, Examiner Mayes emphasized the fact that Applicant needed to show that the instant specification supported the new recitation and, if so, that this was clearly made of record. Mr. Shoop said that he would take everything under consideration and file an amendment in the very near future..

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/DIONNE W MAYES/ Examiner, Art Unit 1747	
---	--

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

(51) Int.Cl. ⁵	識別記号	庁内整理番号	F I	
A 6 1 M 11/00		7720-4C	A 6 1 M 11/00	A
15/00		7720-4C	15/00	Z

審査請求 未請求 予備審査請求 有 (全 22 頁)

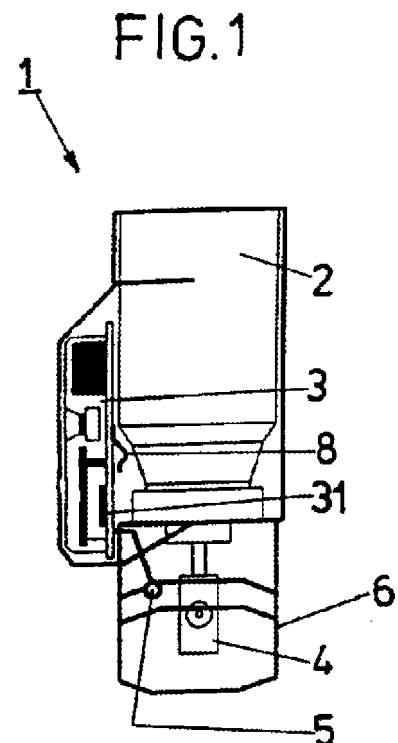
(21) 出願番号 特願平8-502781
 (86) (22) 出願日 平成7年(1995) 6月21日
 (85) 翻訳文提出日 平成8年(1996) 12月27日
 (86) 国際出願番号 PCT/EP95/02410
 (87) 国際公開番号 WO96/00595
 (87) 国際公開日 平成8年(1996) 1月11日
 (31) 優先権主張番号 P4422710. 8
 (32) 優先日 1994年6月29日
 (33) 優先権主張国 ドイツ (DE)
 (81) 指定国 EP(AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, M C, NL, PT, SE), AU, BR, CA, JP, M X, US

(71) 出願人 ベーリンガー インゲルハイム コマンデ
 イトゲゼルシャフト
 ドイツ連邦共和国 デー55216 インゲル
 ハイム アム ライン (番地なし)
 (72) 発明者 ネール クラウス
 ドイツ連邦共和国 デー55128 インゲル
 ハイム アム ライン タンネンヴェーク
 5
 (72) 発明者 シュブレンガー ハーラルト
 ドイツ連邦共和国 デー55218 インゲル
 ハイム アム ライン アイザナッハー
 シュトラッセ 11
 (74) 代理人 弁理士 中村 稔 (外6名)

(54) 【発明の名称】 エーロゾル吸入器

(57) 【要約】

温度センサ(5)が霧化ノズル(4)の領域に配置されているエーロゾル吸入器であって、前記センサが、作動要素が作動させられて吸入動作が引き起こされた後、引き続き起こる推進剤の膨張による冷却を検知する。作動および冷却は、電子モジュール(3)によって、電子的に検出される。技術および治療用のデータを信号から得ることができ、このデータが、ディスプレイユニット及び/或いはアラーム装置を介してユーザに伝えられ、所望の方法による治療に影響を及ぼす。



【特許請求の範囲】

1. 推進剤と該推進剤内に散らされた吸入すべき医薬品とからなるエーロゾルのため供給容器を備え、かつ、作動要素を備え、さらに、内部に空気通路を有するマウスピースを備えた吸入器であって、作動要素の作動に引き続いて、エーロゾルが供給容器からノズルを通してマウスピースの空気通路に入り、医薬品の能動的な吸入が可能になる吸入器において、電子モジュール（3）を備え、該電子モジュール（3）が、モニタ機能用電子ユニット（31）を有し、該電子ユニット（31）が、ノズル（4）の流れ領域に配置された少なくとも一つの温度センサ（5）からの信号と作動を認識する装置（8）からの信号とを供給され、前記吸入器が、更に、前記評価電子ユニット（31）による評価結果の出力用表示装置（34）を備えていることを特徴とする吸入器。
2. 評価電子ユニット（31）が、霧化が起こらないときに、警告信号を発生させることを特徴とする請求の範囲第1項に記載の吸入器。
3. 前記温度センサ（5）が、吸入開始時に、通過する空気を検知し、対応する信号を評価電子ユニット（3）に送り、評価電子ユニット（3）が、患者のための調和した助けとして、視覚的および／あるいは聴覚的に表わされる信号を生成することを特徴とする請求の範囲第1項または第2項のいずれか1項に記載の吸入器。
4. もう一つの温度センサをエーロゾルの流れ通路に配置し、前記もう一つのセンサが、電子評価ユニット（31）に送られ第1の温度センサ（5）からの信号とリンクされる基準信号を生成し、このリンクの結果により、エーロゾルの放出用が導かれることを特徴とする請求の範囲第1項ないし第3項のいずれか1項に記載の吸入器。
5. 霧化に先立って、温度センサ（5）の周囲温度が検出され、デジタル化され、評価電子ユニット（31）に記憶され、霧化の間、温度変化の時間特性が検出され、温度プロファイルとしてデジタル化され、そして、エーロゾルの霧化量が、後者の信号と前に記憶されていた周囲温度との間の差の適当な極限值間における積分値から、導かれることを特徴とする請求の範囲第1項ないし第3項

のいずれか1項に記載の吸入器。

6. 評価電子ユニット(31)が、メモリと、これを通してデータを外部から前記メモリに入力し且つ前記メモリからデータを読み出すシリアルインターフェイスとを備えた、マイクロコントローラあるいは特注回路で構成されていることを特徴とする請求の範囲第1項ないし第5項のいずれか1項に記載の吸入器。

7. 前記供給容器(2)が吸入器に着脱自在に挿入可能であり、その外側に光学的にコード化された表面を備え、前記電子モジュール(3)が前記コードが示す情報を解読できることを特徴とする請求の範囲第1項ないし第6項のいずれか1項に記載の吸入器。

8. 交換可能な供給容器(2)が電子メモリを有し、該メモリに記憶されたデータを前記評価電子ユニット(31)が読出し可能であり、かつ、前記評価電子ユニット(31)がデータを前記メモリに入力可能であることを特徴とする請求の範囲第7項に記載の吸入器。

9. 前記交換可能な供給容器(2)が、EEPROMモジュールを備えていることを特徴とする請求の範囲第8項に記載の吸入器。

10. 前記温度センサ(5)からの信号が、該信号が作動要素を作動させて自動的に吸入行程を引き起こすような方法で、評価されることを特徴とする請求の範囲第1項ないし第9項に記載の吸入器。

11. 請求の範囲第1項ないし第10項に記載の吸入器の機能をモニタする電子モジュールであって、前記吸入器に着脱自在に取付け可能であり、それ自身から離れるように突出し、少なくとも一つの温度センサ(5)を備え、吸入器(1)に連結された後、前記センサ(5)が、前記ノズル(4)の開口に近接して当接することを特徴とする電子モジュール。

12. 第2の温度センサが配置されていることを特徴とする請求の範囲第11項に記載の電子モジュール。

13. 温度センサ(5)が、NTC抵抗器、サーミスタあるいは表面熱電対であることを特徴とする請求の範囲第11項または第12項のいずれか1項に記載の電子モジュール。

エーロゾル吸入器

本発明は、吸入すべき医療物質（医薬品）用のエーロゾル吸入器に関し、かつ、そのような吸入器に関連に使用される電子モジュールに関するものである。

エーロゾル吸入器は、吸入すべき所定量の医薬品を患者が能動的に吸い込むのを助ける器具である。このような器具の典型的な使用例は、急性の喘息発作である。対応する作動要素を作動させると、推進剤と、この推進剤の中に存在しかつその中に分散している医薬品とからなるエーロゾルが、供給容器から、ノズルを通して、マウスピース内のエアーチャネルにはいり、そこで、エーロゾルは患者によって能動的に吸入される。エーロゾルの放出および霧化を、電子的あるいは機械的に起こすことができる。

以前は、作動要素の作動時に、実際に霧化が起こったか否かを検出することは不可能であった。例えば、ノズルの障害によって、霧化が起こらないことがある。エーロゾル供給容器が空のときにも、当然、霧化は起こらない。患者は、急性発作を抑えるのに必要な薬を吸入しているので、実際は、事実でないか或いは一部分だけが事実かもしれないが、このことにより余病が併発されることがある。所定量の一部のみの供給が、しばしば、行われると、患者は、更に吸引することによって医薬品の効果を増そうとする。これは危険な状況をもたらし、その結果、過量摂取が起こることがある。さらに、患者を治療している医師が、所定の時間間隔内に投与した投与回数の概略が分からなくなってしまい、確実な治療の妨げとなってしまう。

このような背景の下、本発明の目的は、少なくとも、作動要素を作動させた時、エーロゾルの霧化を確実に認識かつこれを評価即ち活用することができるタイプのエーロゾル吸入器をさらに改良することである。更に、本発明によれば、投与された回数、供給容器内に残っている投与量およびその表示のような処置パラメータに関連する一連の評価、更に、例えば、医師の処方箋に対応しているかどうかを決定するためのエーロゾルのチェックが可能である。更に、そのような吸入

器と関連して使用するために電子モジュールが設けられることになり、この電子モジュールは、本発明の目的の電子部品として満足のいくものであるが、原則として、公知の全てのエーロゾル吸入器に対しても、エーロゾル吸入器の付属品として使用できる。

この目的は、請求の範囲第1項の特徴部分の特徴を備えた吸入器、および、請求の範囲第8項による電子モジュールによって達成される。

有利な改良例が、関連する従属項に記載されている。

本発明によれば、電子モジュールを備えた吸入器が提供され、該電子モジュールは、ノズルの流れ領域に配置された少なくとも1つの温度センサからの信号および作動要素の作動を認識する装置からの信号を供給される、機能モニタ用評価電子ユニットを備えており、さらに、評価電子ユニットによって生成された評価結果の出力を表示する装置を備えている。

本発明の要点は、エーロゾルの霧化が起こるノズル内に温度センサを直接配置したことである。このことにより、推進剤の冷却が温度センサを冷却し、明確に規定された電気信号を生成できるので、作動の認識および霧化時における推進剤の冷却に基づいたエーロゾル霧化の能動的検出が可能となる。その結果、ノズル内に障害があったり、あるいは、エーロゾル供給容器が空であるといった機能不全を、確実に検出できる。

特別かつ簡単な実施態様では、評価電子ユニットが、霧化が起こらないときに警告信号を生成し、そして、供給容器内にまだ収容されている吸入投与量の数を示す信号を生成する。これらの信号は、適当な表示装置によって、警告の場合には、聴覚信号で、患者に伝えられる。霧化をモニタしているので、供給容器が空であったり、あるいは又、特に、ノズルに障害があったときに起こるように、霧化が起こらず医薬品を吸入しなかった場合には、使用者に警告を与えることができる。

さらに有利な態様では、温度センサが、吸入の開始時に、通過する空気流を検出し、これに対応する信号を発生させ、この信号が評価電子ユニットに送られ、評価電子ユニットが、吸入行程において患者を助けるために、光学的かつ／あるいは音声的に示される信号を生成する。

この更なる態様の背景は以下の通りである：

エーロゾルの正確な吸入は、理想的には、以下のようにおこなわれる、即ち、患者は、息を吐いてから、器具を口に当て、吸入を開始した後に、作動要素を押して、霧化を引き起こす。しかしながら、多くの使用者にとって、呼吸と霧化を引き起こすことを調整することは難しい。しかしながら、呼吸と霧化引き起こしとのタイミングが合わないと、薬剤による治療の効果が減少し、治療効果が損なわれる。吸入開始の直後に、患者が、視覚的表示あるいは聴覚的表示によって霧化が差し迫っていることを知らされるという点で、上述した更なる実施態様は有効である。このようにして、処置の臨床的効果が、著しく向上する。

別の実施態様では、もう一つの温度センサがエーロゾル流路の外側に配置されており、このもう一つの温度センサが基準信号を生成し、この基準信号が、同様に、評価電子ユニットに送られ、第1の温度センサからの信号と関連付けられ、この結果により、放出されたエーロゾルの量が、導き出される。この関連付けは、例えば、ノズルに直接配置された第1の温度センサと周囲温度との間の相違の時間特性を形成することができる差動増幅器で行うことができる。次いで、下流側の評価電子ユニットが、この差の信号を受け、適当な極限值間での、この信号のインテグレーション（integration）すなわち積分値が、評価電子ユニットのメモリ内に記憶された関連する事項の助けて、エーロゾルの霧化量になる値を与える。量的な検出を行っているので、患者は、吸入を行う度に、更に吸入する必要があるか否かについての正確な情報を得ることができる。評価電子ユニットのプログラム内に設定されている特定量に届かない場合には、吸入された活性成分が少なすぎることを患者に知らせる警告信号を出してもよい。このようなモニタが可能であるということにより、吸入器を使用する際の信頼性が高くなり、治療がより効率的になる。

他の実施態様として、霧化に先立って、ノズルの領域に配置された温度センサの周囲温度を検出し、デジタル化し、評価電子ユニットに記憶できるので、エーロゾルの放出量を決定できる。吸入中に、エーロゾルを霧化させたとき、センサの温度変化の時間特性を、所謂温度プロファイルとして検出する。この温度プロファイルをデジタル化し、この値から、予め記憶しておいた周囲温度を除する。

適当な極限值間での差の積分値が、評価電子ユニットのメモリ内に記憶された関連事項の助で、エアロゾルの霧化量となる値を与える。センサ信号増幅器の出力電圧とセンサの温度との関係を、評価電子ユニットのメモリ内に記憶させることができる。センサおよび信号増幅器の非線形性、および、周囲温度の変化によって生じる作動点のシフトの影響を、評価電子ユニット内で、計算により排除することができる。

他の実施態様において、もし評価電子ユニットがマイクロコントローラを備えているなら、データ記憶用のメモリおよび外部コンピュータとの接続用シリアルインターフェイスを備えているのが好ましい。

この実施態様により、担当の医師は、関連する分野では全く初めて、医師が決めた吸入投与回数を患者が本当に吸入した否かおよび吸入器が行われている時間間隔をモニタできることになる。多量のデータをメモリにインプットすること、及び、これに関連する機能が可能である。このように、例えば、医師は、次の吸入を行うまでの時間間隔を予め定めることができ、モジュール内の実時間（リアルタイム）のクロックにより、視覚的および／あるいは聴覚的な信号を出して、患者に次の吸入を思い出させることができる。

この機能をモニタすることができ、そして、この機能の実行あるいは不実行を同様にメモリに記憶させることができる。担当の医師が次に来たとき、このデータは、シリアルインタフェイスを介して読み出され、医師によって解読される。メモリへの入出力のために、電子モジュールは、上述したように、シリアルインタフェイスを介して、外部コンピュータに接続されるように構成されることになる。

本発明による吸入器の評価電子ユニットの存在により、別の機能を簡略化でき、もう一つの実施態様では、エアロゾル供給容器が、吸入器に着脱自在に挿入可能な、交換可能部品であるようにすることができる。着脱自在な供給容器の外側に、例えば、写真のフィルムカートリッジの所謂DX-コード(DX-coding)と関連して知られているような光学コード化面を設けることができる。評価電子ユニットが、このコードが示す情報を解読できるように設計されている。この情報は、例えば、エアロゾル内の医薬品の活性成分のタイプおよびその期限を表してい

る。

このデータは読み出されて、評価電子ユニットのマイクロコントローラ内で、例えば、医師が入力した活性成分のタイプに関連する情報と比較される。両者が異なっている場合には、警告信号を発するように構成することができる。上述した電子モジュール内のリアルタイムのクロックを、エーロゾル内の医薬品の期限データをチェックして、期限が過ぎたときに、警告を発するために使用できる。

この実施態様では、交換可能な供給容器は、それ自身が、電子メモリを備えており、このメモリも記憶されたデータを評価電子ユニットが読み出し、かつ、評価電子ユニットがデータをこのメモリに入力できるように構成してもよい。このメモリは、上述した光学コードに加えて設けても、或いは、メモリだけを設けてもよい。吸入器と外部コンピュータの間のデータ交換のために、例えば、医師の前提で、電源無しでデータを保持する差し込み型EEPROMモジュールを使用してもよい。外部コンピュータは、これを介して、EEPROMモジュールにデータを入出力できるアダプタを有している。この記憶モジュールを介して、一方では、活性成分に関する情報及び処方された処置を器具に伝達することができ、他方では、器具それ自身に、実際の治療データを入力できる。

さらに別の実施態様として、センサ接触子を吸入器のマウスピースに配置してもよい。センサ接触子からの信号は、評価電子ユニットに送られる。このようにして、正しい霧化の場合に、患者が実際に医薬品を受入れているか否かをチェックできる。これにより、正しいが、空間に開放されて患者に到達しなかった霧化は、確実に、投与された投与量としてメモリに記録されない。

エーロゾルが霧化するノズルに直接設けられた温度センサを吸入器が備え、作動要素の作動を認識する装置を備え、かつ、センサからの信号および作動認識装置からの信号を評価する評価電子ユニットを備えていることによって、上述したモニタが可能であることを強調しておく。実際の吸入器とは独立して取扱われ、且つ、それ自身が商品である、導入部で言及した電子モジュールは、本発明によって、吸入器に着脱自在に固定できる別体のハウジングを備え、また、それ自身から離れて突出する少なくとも一つのセンサを備え、このセンサは、吸入器のノ

ブル開口のすぐ近傍に配置されている。

電子モジュールは、吸入器とは別に、製造し且つ試験することができる。電子

モジュールは、製造の最終段階において初めて、吸入器に取付けられ、完成品が最終試験を受ける。しかしながら、電子モジュールを、具体的な吸入器とは別に独立して流通させ、付属品として提供することもできる。

さらに別の実施態様では、上述した第2の温度基準センサを電子モジュールに配置し、これによって、ユニット全体が、第2のセンサが、例えば吸入器に、つけられていないときと同じように、大変コンパクトになり、これは勿論、電気的接続を行うことを必要とすることになる。

温度センサは、NTC抵抗器、サーミスタあるいは表面熱電対のような電気的特定が、温度変化によって、評価できるように変化する素子であるのが好ましい。

評価電子ユニットは、必要な全ての電子的機能が集積されたマイクロコントローラあるいは特注回路で構成するのがよい。この設計により、評価電子ユニットおよび電源要求のために必要なスペースの減少が可能になり、これは、バッテリーの容積および電子モジュールの全体の容積が、関連して減少するからである。SMD技術で回路板を構成するのがよい。スペースおよびコスト上の理由から、チップオンボード(chip-on-board:COB)あるいはテープ自動化接着(tape-automated bonding)技術によって、ICハウジングを使用することなく、マイクロコントローラを組立てるのがよい。表示ユニットおよび必要なバッテリーは、クリップ留め式プラスチックフレームを介して、回路板に固定され、導電性ラバーおよび接触パネを介して回路板に電気的に接続されている。

吸入器のキャップの脱着によって、追加の操作行程なしで、器具スイッチのオンオフを行うことができる。もしキャップが比較的長時間開いたままであるなら、電子ユニットは、所定時間経過後、自動的に所謂”スリープモード”に切り替わり、吸入を引き金にして、自動的に、”起こされる”。キャップが適所にあるときには、霧化が起らないように機械的にロックされている。

表示ユニットは3ディジット7セグメントディスプレイと、日常の投与量警告、

電源警告および故障表示のための符号とを備えたLCDからなるのが好ましい。

新たに充填したエロゾル供給容器を吸入器に挿入すると、電子モジュールのリセット用押しボタンを作動させ、残りの投与量を、満タンの容器に対応する値に設定する必要がある。この機能は、他の実施態様にしたがって、すなわち、作

動要素が作動させられた時および容器が交換された時のいずれの場合にも、信号を評価電子ユニットに送る作動認識装置によって、実施することもできる。

本発明による吸入器の吸入工程が、電子的に起こるように構成してもよい。この目的のために必要な電子ユニットを、同様に、電子モジュール内に収容することができる。マウスピースに設けられたセンサ接触子によって、誤作動を防止する。

上述したように、ノズルの流れ領域に設けられた温度センサによって吸入過程を電子的に認識することを、呼吸によって完全に自動的に霧化を、起こすために利用することができる。この目的で、対応する信号を評価した後で、評価電子ユニットが、吸入器の作動要素に信号を送り、霧化を起こす。したがって、器具によって、調和が完全に確保される。患者は、ただ、器具を口にあて、息を吸うだけでよい。

センサからの信号の評価は、以下のようにして行われる、即ち、増幅後に、アナログ信号を直ちにデジタル化し、上述した比較器の機能は、評価電子ユニットのプログラムによって保証され、対応する切り換えレベルおよび遅延時間が、プログラムによって決定される。

以下、本発明による吸入器の実施態様を詳細に説明する。添付図面において、図1は、横方向に取付けられた電子モジュールを備えた吸入器の正面図であり、

図2は、図1の吸入器の側面図であり、

図3は、図1および図2の器具の平面図であり、

図4は、評価電子ユニットの主要回路の線図であり、

図5aないし図5cは、出力信号の時間特性を示し、

図6は、ノズル開口に設けられたセンサと基準センサの間の差信号の積分値の

時間特性を示し、

図7は、吸入行程を電子的に評価する場合の出力信号の時間特性を示している。

図1ないし図3は、本発明による吸入器の図面であり、これらの図面は、主要な線だけが示され、正確な断面には対応していない。

本発明による吸入器1は、エーロゾル用の供給容器2を備えている。本実施態様においては、供給容器2は、ハウジングに着脱自在に取付けられており、ハウ

ジングは、空気通路7が内部に延びているマウスピース6を備えている。(図示しない) 作動要素によって、投与量のエーロゾルが、供給容器2からノズル4に入り、そこで霧化される。患者は、空気通路7を通して、この霧化エーロゾルを吸う。

この行程中、供給容器2は動き、作動認識装置8を介して信号を発生させ、この信号が、評価電子ユニット31に送られる。第1の温度センサ5が、ノズル4の開口に直接配置されている。ノズル4からの霧化が起こると、推進剤が膨張して、ノズル開口の領域の温度が下がる。この温度低下を温度センサ5が検知し、温度センサ5が、対応する信号を生成して、この信号が、同様に、評価電子ユニット31に送られる。

上述したように、本実施態様では、電子モジュール3が、吸入器1にクリップ留めされ、独立して取り扱えるようになっている。これはコンパクトな構成のものであり、全ての必要な構成要素を収容しており、これらのうち、バッテリー36および光学表示ユニット34が、図1ないし図3に、参照番号を付されて示されている。この光学表示ユニットは、3ディジット7セグメントのLCD表示装置であるのが好ましい。評価電子ユニット30の主要回路の線図を、図4に示す。

本実施態様においては、主要構成部品は、評価電子ユニット31であり、このユニットに、作動認識装置8からの信号および温度センサ5からの信号が送られる。評価電子ユニットは、接点33が閉じられるまで作動されず、これは、器具のキャップが外されたときに起こる。

この回路は、バッテリー36から電気を供給される。本実施態様では、上述した

表示ユニット 3 4 によって表示が行われる。

更に、リセットスイッチ 3 5 が設けられており、これは新たに充填された供給容器が吸入器 1 に挿入されたとき作動させられ、残り投与量が、評価電子ユニット 3 1 のメモリ内で、満タンの供給容器に対応する値に設定される。

信号処理を、図 5 および図 6 を参照して、簡単に説明する。

図 5 a は、温度センサ 5 の電圧 U_1 の曲線を示す。ノズル 4 内で推進剤が膨張し、これに伴って、センサ 5 が冷却されると、電圧 U_1 は初めは、急激に上昇し、霧化行程の後、熱的な時定数に従って、その初期値まで落ちる。

図 5 b は、入口に図 5 a の電圧 U_1 が与えられる周波数分離増幅器の出力電圧 U_2 の時間特性を示す。霧化の場合に、 U_2 が明確なパルスを有していることがわかる。

電圧 U_2 は、例えば、休止状態で一定の正の出力電圧を有し正しい霧化が行われてるときには、負のパルスを出し、そのとき、一時的に、電圧を確実に 0 にする比較器に供給される。電圧 U_3 は、評価電子ユニットに対するデジタル入力信号である。増幅器および比較器を、評価電子ユニットの一部分として形成してもよい。

図 6 は、周囲温度にさらされている基準センサとしてもう一つの温度センサ（図示せず）を設けたときの、電子的評価の可能性を示す。差動増幅器を使って、周囲温度と吸入器 1 のノズル 4 の温度との差の時間特性を導き、この時間特性を、マイクロコントローラ内に収容されたプロセッサのアナログーデジタル変換器に送る。図 6 における適当な極限值 t_1 及び t_2 の間の信号 U_1 の積分値が、変数

$$Q' = \int_{t_1}^{t_2} u_1(t) dt$$

を与え、この変数が、プロセッサの ROM 記憶装置モジュール内に記憶された明確に規定された関連する値の助けによって、実際のエーロゾル霧化量 Q になる。

最後に、図 7 は、吸入行程の認識が電子的に評価される、他の実施態様による信号処理を示す。

霧化認識用に設けられた周波数分離増幅器を、信号処理のために使用するの

好ましい。

図 7 a は、温度センサの電圧 U_1 の時間特性を示し、図 7 b は、分離増幅器の出力における電圧 U_2 の特性を示し、図 7 c は、霧化認識用の比較器の出力における電圧 U_3 を示し、図 7 d は、吸い込みおよび正しい霧化を伴った吸入行程のためのもう一つの比較器の出力における電圧 U_4 の時間特性を示す。

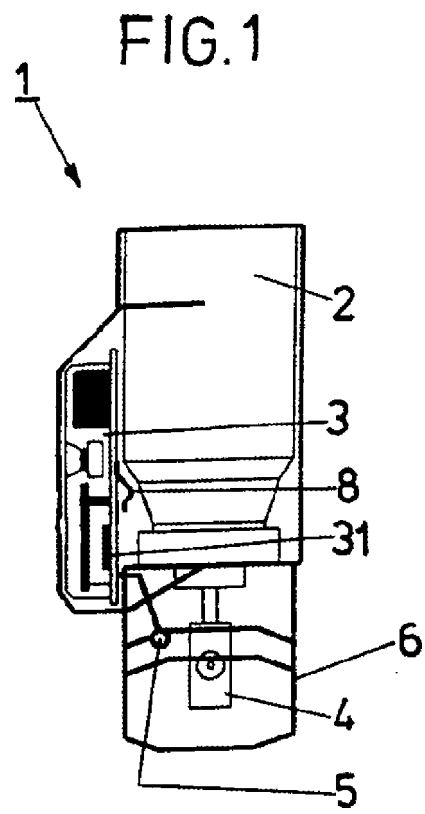
温度センサの電圧 U_1 は、最初に、小さなパルスを有し、このパルスの前側が、

吸入の開始、即ち、最初の吸入空気が温度センサ 5 を通過したことを示す。しかしながら、周波数分離増幅器の出力電圧 U_2 は、すでに、極端に目立つパルスを有している。この電圧は比較器に送られ、比較器の出力電圧 U_4 が、評価電子ユニット 31 用のデジタル出力信号である。電圧 U_4 の前側面は、吸入 (t_0) の開始と同時に起こる。評価電子ユニット 31 のプログラム内で、この側面に対して自由規定された遅延時間の後、評価電子ユニット 31 は、電気機械変換器（例えば圧電発振器）を介して聴覚信号を発する。

電圧 U_1 の、即ち、より強い正の上昇、および、強い負のパルスを備えた電圧 U_2 の連続推移は、引き起こしに続くエーロゾルの正しい霧化による、温度センサ 5 の冷却の結果である。対応する比較器の出力電圧 U_3 は、負のパルスを有しており、これが、評価電子ユニットに送られる。

口を吸入器につけてから吸入を行い、かつ、信号を聞くまでは、作動要素を作動させて霧化を引き起こさないことで、患者にとって取扱いが簡単である。これは、患者が、例えば吸入器に口をつけ吸い込んだ直後に霧化を起こさないことを確実にし、あるいは、吸入行程が終わったときにはスイッチを入れないが、正しく吸入を伴っているときには霧化を引き起こすことを確実にする。これは、治療に好ましく影響する。

本発明は上述した実施例に限定されるものでなく、検出したデータの使用および評価に関連する上述した全ての可能性を含むものである。



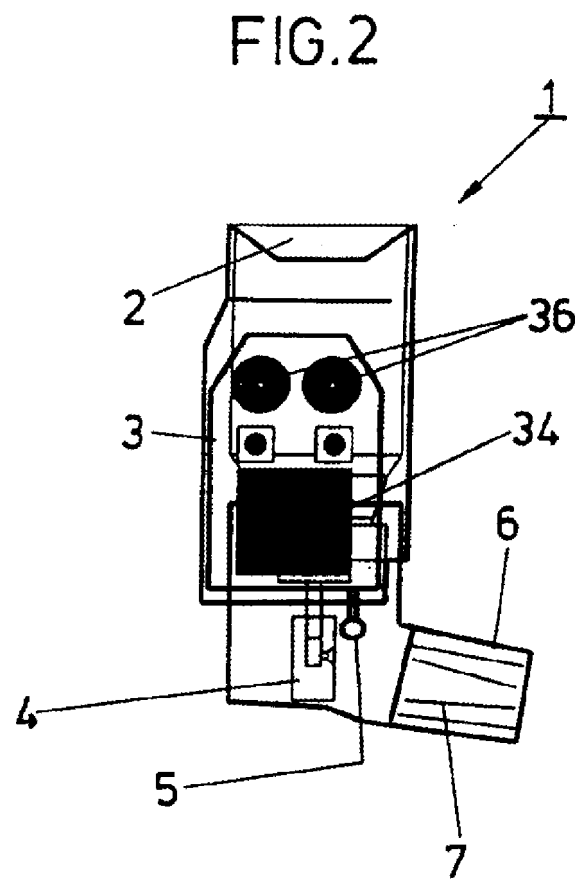
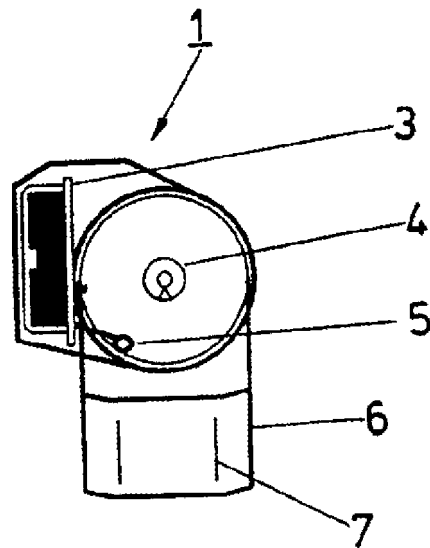


FIG.3

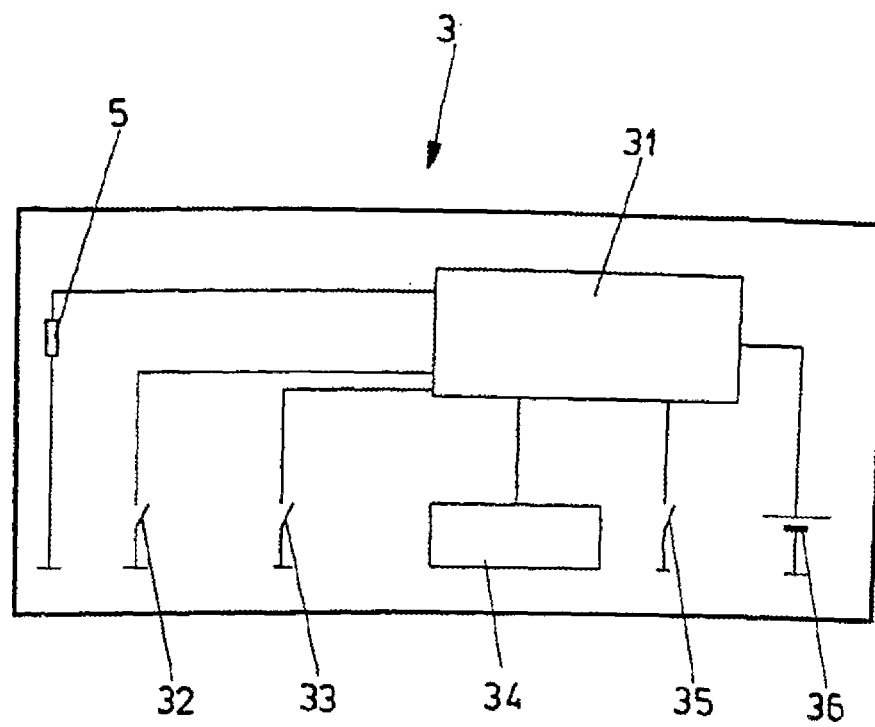
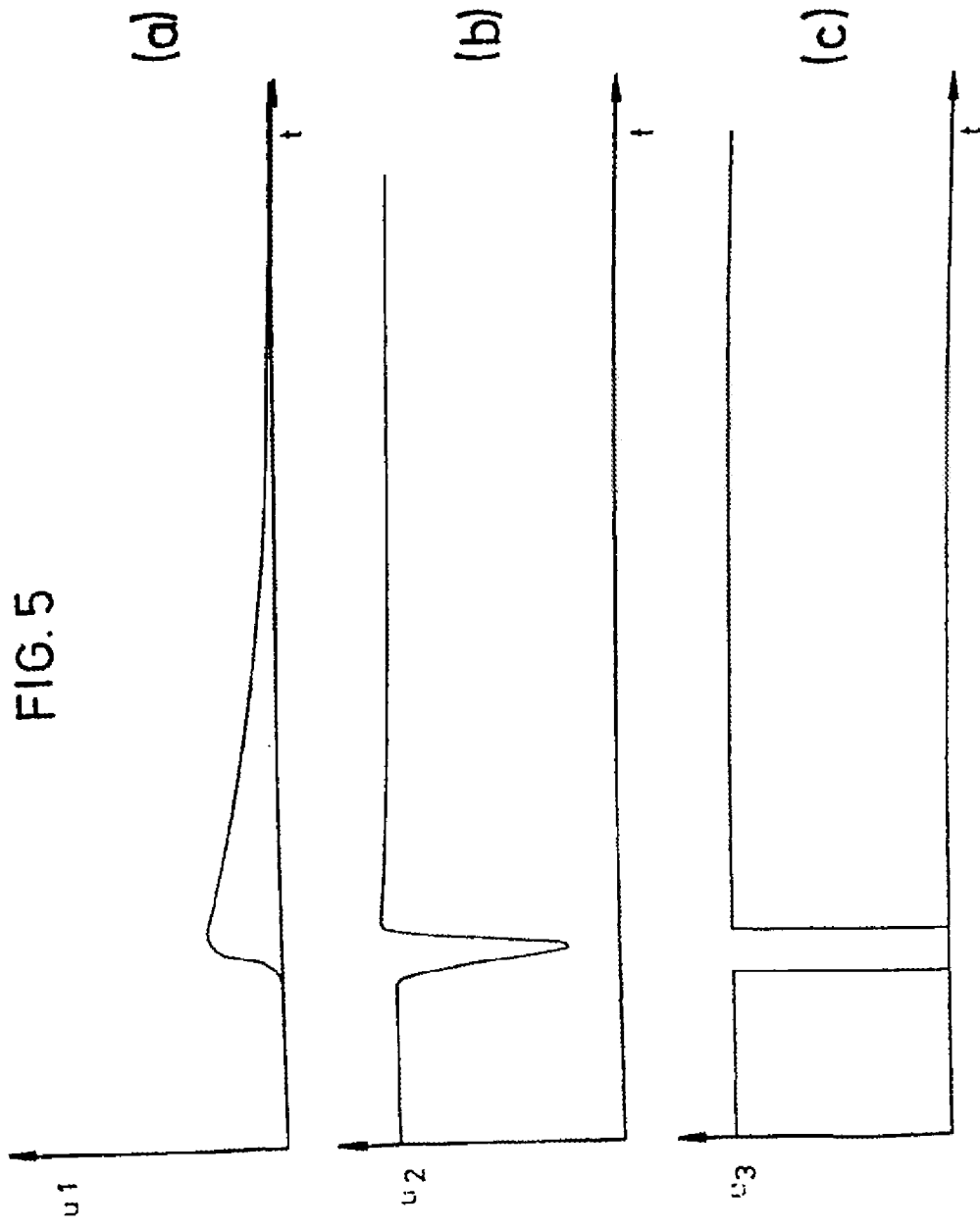


FIG. 4



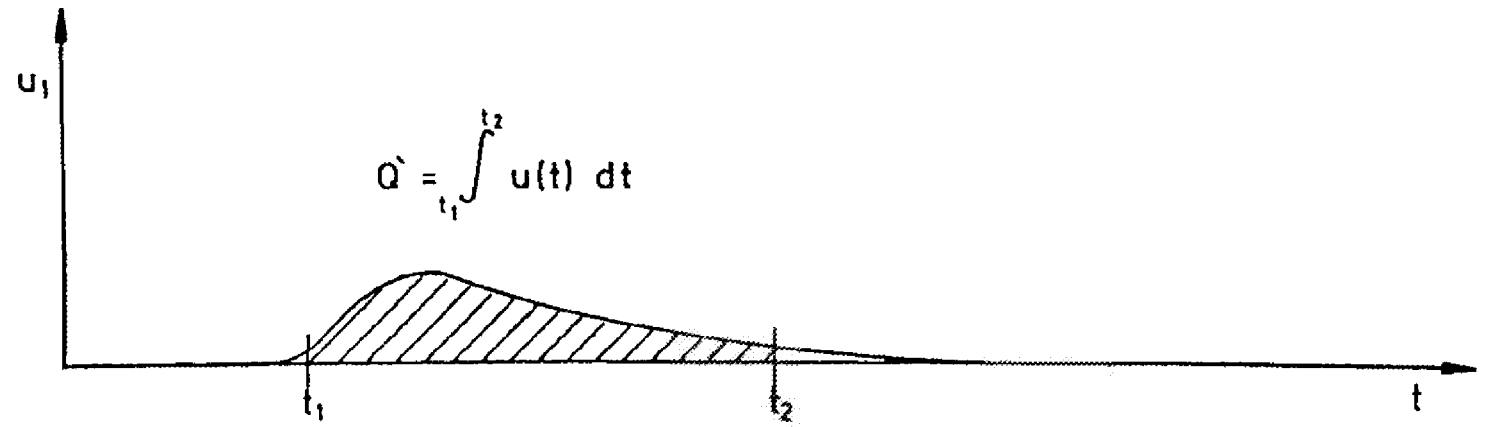
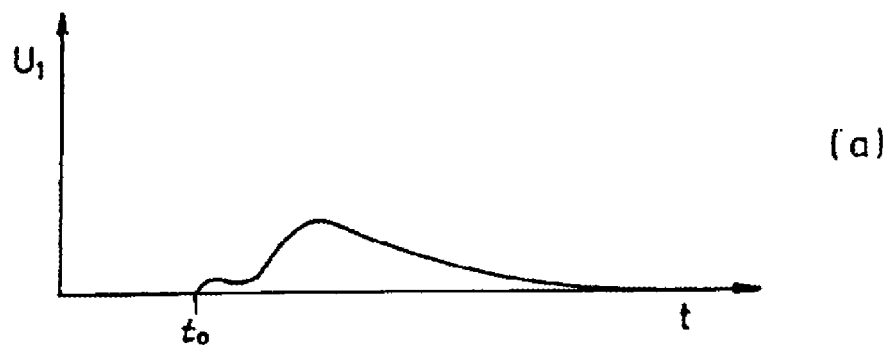
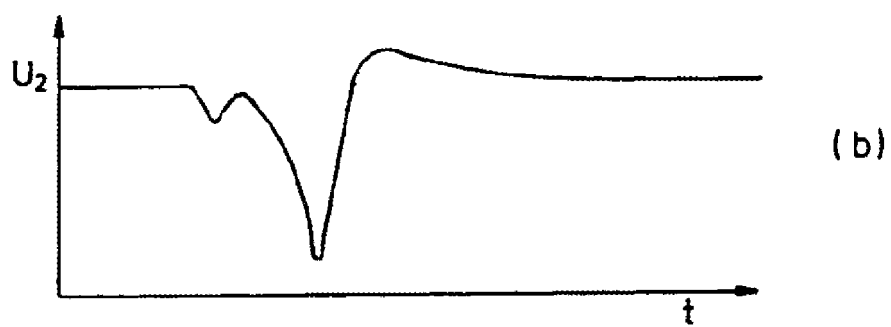
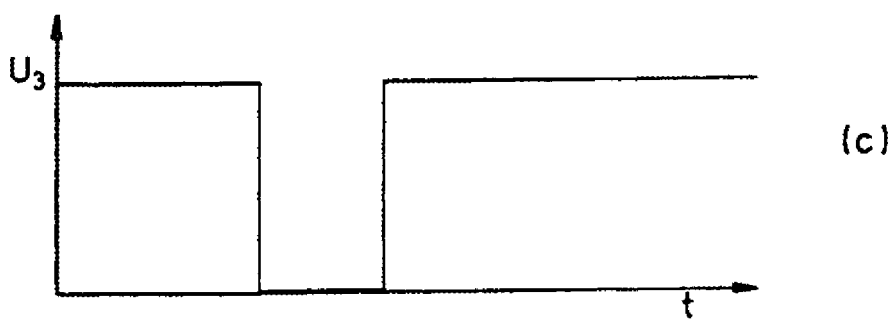
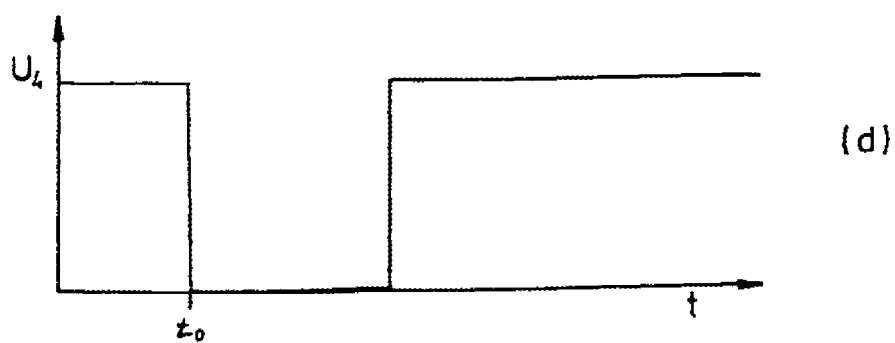


FIG.6

FIGUR 7



INTERNATIONAL SEARCH REPORT

 Int. Application No.
PCT/EP 95/02410

 A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,92 07599 (MINNESOTA MINING & MFG) 14 May 1992 see abstract; figure 1 see page 13, line 1 - page 14, line 10 see page 19, line 6 - line 31 ---	1-13
Y	US,A,5 284 133 (BURNS JAMES S ET AL) 8 February 1994 see abstract; figure 4A see column 7, line 51 - column 10, line 34 see column 12, line 3 - line 31 ---	1-13
A	WO,A,92 15353 (MIRIS MEDICAL CORP) 17 September 1992 see abstract; figure 1 see page 29, line 6 - page 30, line 33 --- -/-	1,4

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

27 September 1995

Date of mailing of the international search report

17.10.95

Name and mailing address of the ISA

 European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax (+31-70) 340-3016

Authorized officer

Zeinstra, H

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int. l. Application No.
PCT/EP 95/02410

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO,A,92 17231 (INNOMED INC) 15 October 1992 see abstract; figure 4 see page 5, line 20 - page 6, line 32 see page 10, line 22 - page 11, line 9 -----</p>	7

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/EP 95/02410

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9207599	14-05-92	EP-A- 0507913	14-10-92
US-A-5284133	08-02-94	NONE	
WO-A-9215353	17-09-92	US-A- 5404871	11-04-95
		EP-A- 0529053	03-03-93
		US-A- 5394866	07-03-95
		US-A- 5450336	12-09-95
		US-A- 5392768	28-02-95
WO-A-9217231	15-10-92	NONE	

Form PCT/ISA/210 (patent family annex) (July 1992)



US006119684A

United States Patent [19][11] **Patent Number:** **6,119,684****Nöhl et al.**[45] **Date of Patent:** ***Sep. 19, 2000**[54] **AEROSOL INHALER**[58] **Field of Search** 128/200.24, 200.14,
128/200.23, 203.12, 204.21, 204.23, 205.23[75] **Inventors:** **Klaus Nöhl; Harald Sprenger**, both of
Ingelheim am Rhein, Germany[56] **References Cited**[73] **Assignee:** **Boehringer Ingelheim KG**, Ingelheim,
Germany**U.S. PATENT DOCUMENTS**

5,284,133	2/1994	Burns et al.	128/200.23
5,331,953	7/1994	Andersson et al.	128/200.14
5,363,842	11/1994	Mishevich et al.	128/200.14

[*] **Notice:** This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).**FOREIGN PATENT DOCUMENTS**

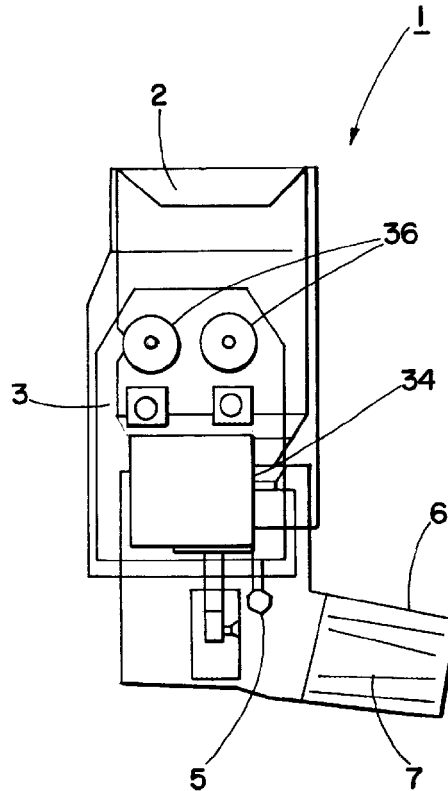
WO9207599	10/1991	WIPO .
WO9215353	3/1992	WIPO .
WO9217231	3/1992	WIPO .

Primary Examiner—Aaron J. Lewis*Attorney, Agent, or Firm*—Robert P. Raymond; Alan R. Stempel; Mary-Ellen M. Devlin[21] **Appl. No.:** **08/765,466**[22] **PCT Filed:** **Jun. 21, 1995**[86] **PCT No.:** **PCT/EP95/02410**§ 371 Date: **Jun. 19, 1997**§ 102(e) Date: **Jun. 19, 1997**[87] **PCT Pub. No.:** **WO96/00595****PCT Pub. Date:** **Jan. 11, 1996**[30] **Foreign Application Priority Data**

Jun. 29, 1994 [DE] Germany 44 22 710

[51] **Int. Cl.⁷** **A61M 11/00**[52] **U.S. Cl.** **128/200.14; 128/200.23;**
128/204.23; 128/205.23[57] **ABSTRACT**

In an aerosol inhaler it is proposed that a thermal sensor 5 be arranged in the region of the atomization nozzle 4, which sensor, following the actuation of an actuating element and the triggering of an inhalation process, undergoes cooling as a result of the expansion of the propellant which then occurs. The actuation and cooling are electronically detected in an electronic module 3. Technical and therapeutic data can be derived from the signal, which data are communicated to the user via the display unit and/or alarm devices and influence the therapy in the desired manner.

1 Claim, 5 Drawing Sheets

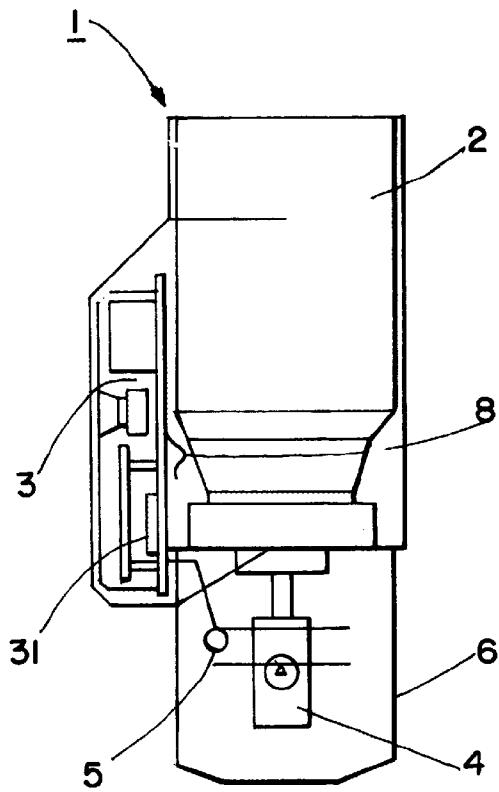


Fig. 1

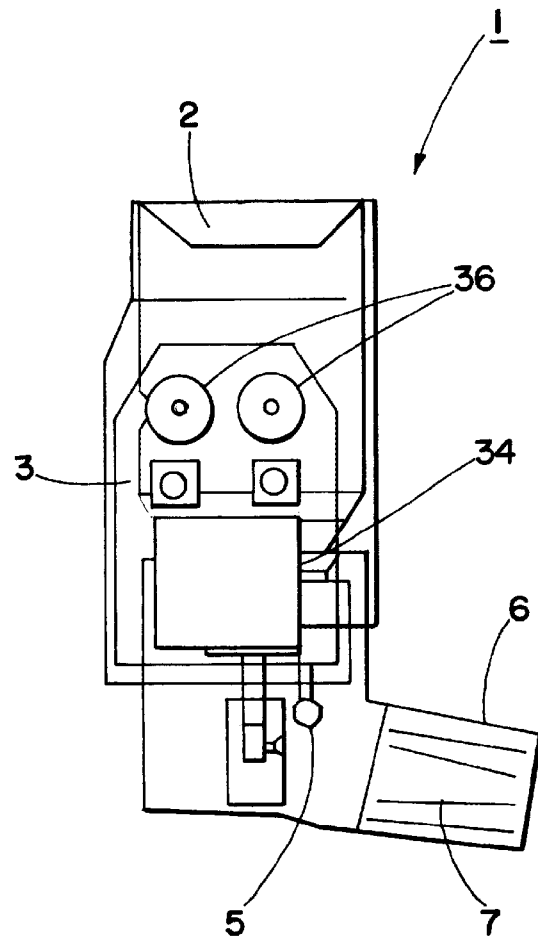


Fig. 2

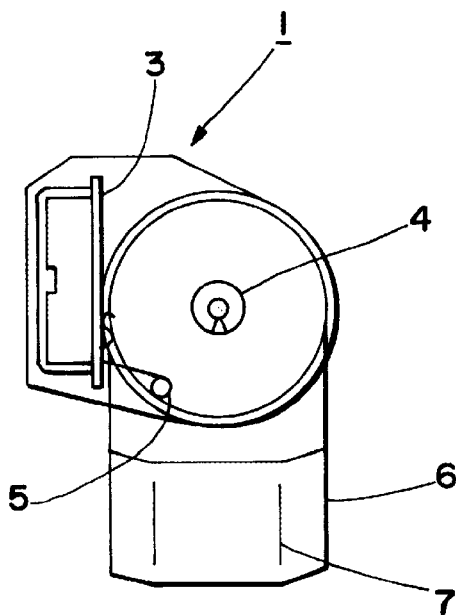


Fig. 3

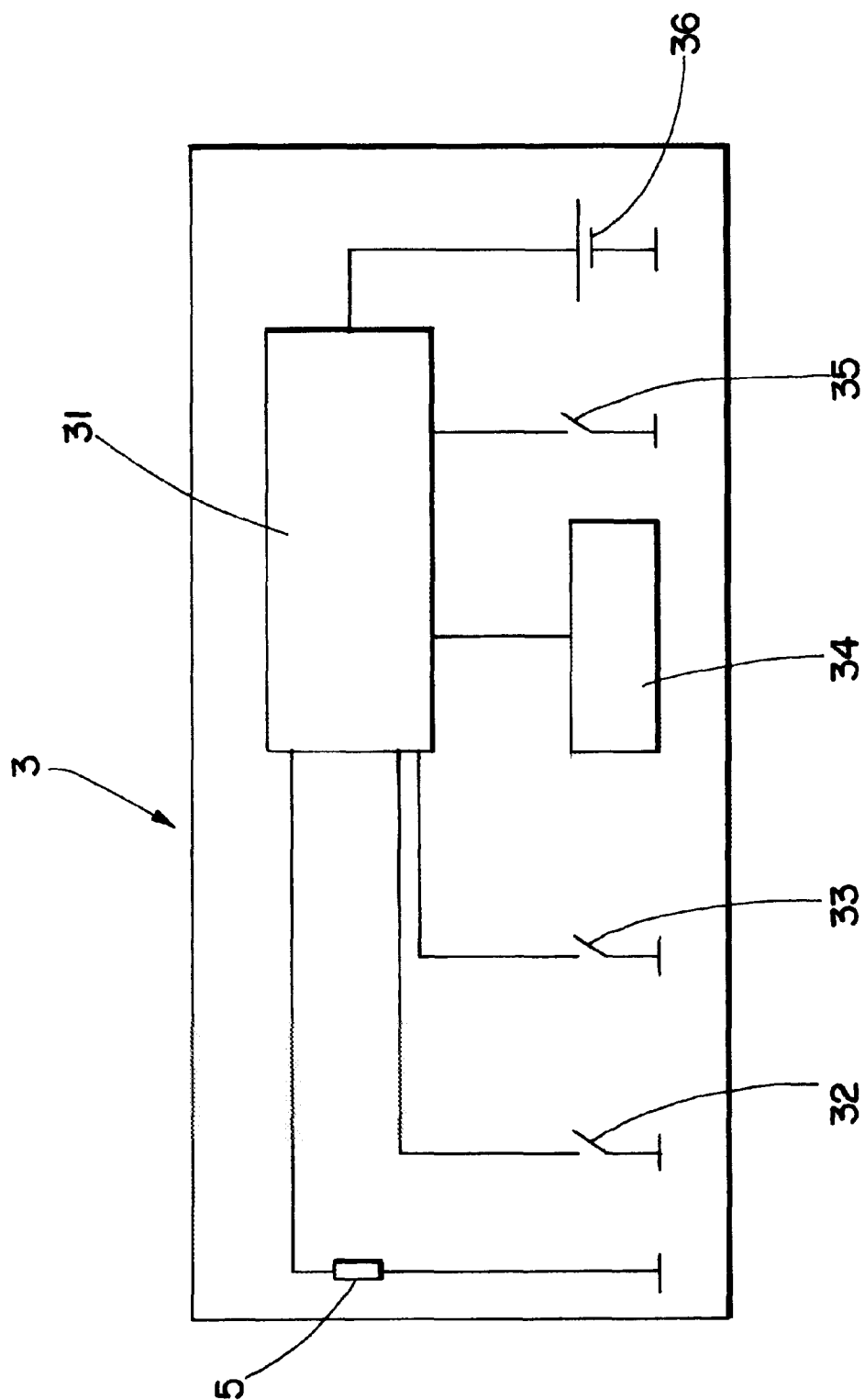


Fig. 4

Fig. 5(a)

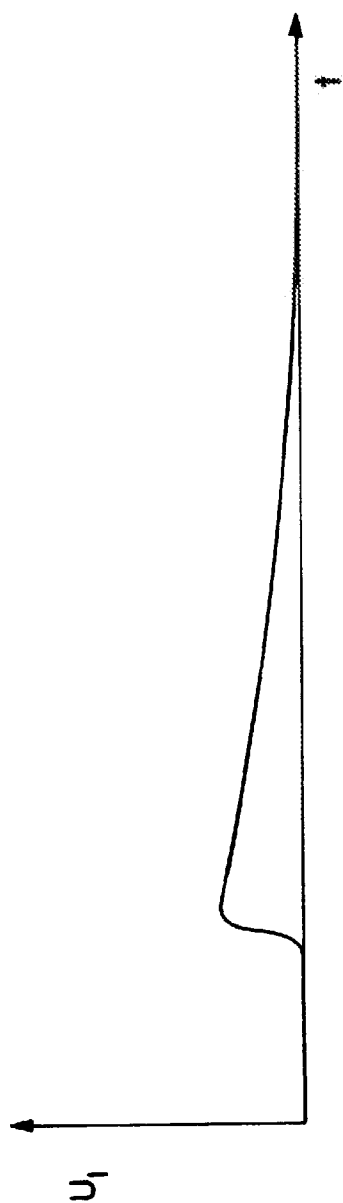


Fig. 5(b)

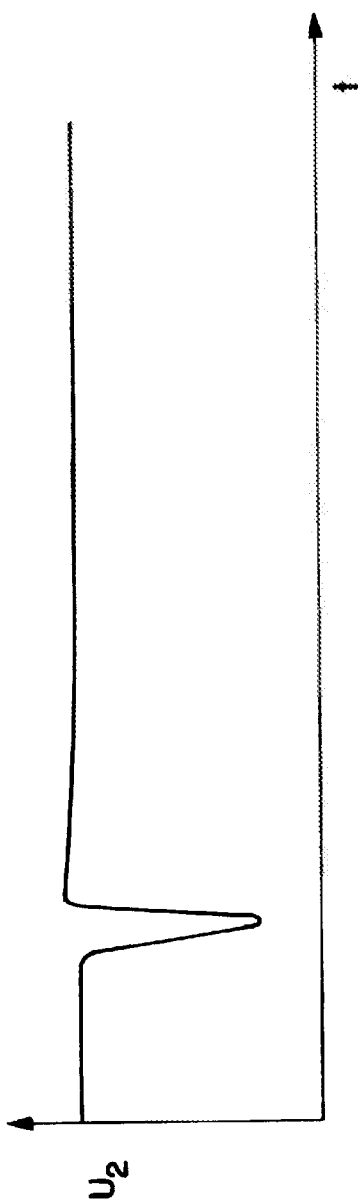
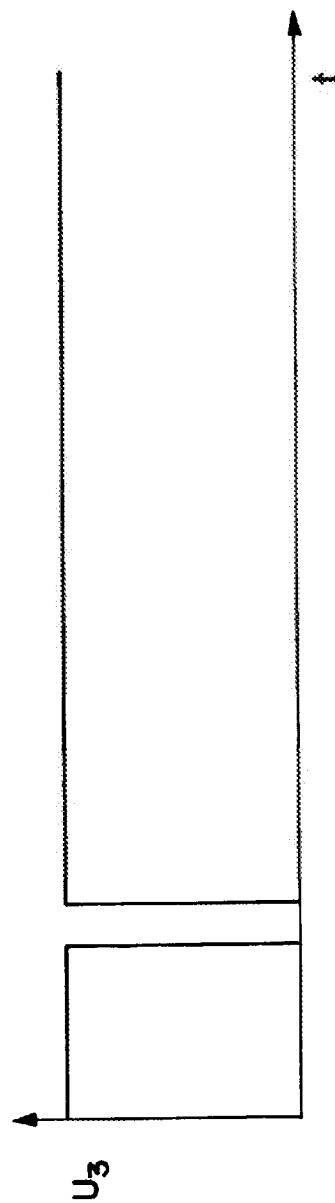


Fig. 5(c)



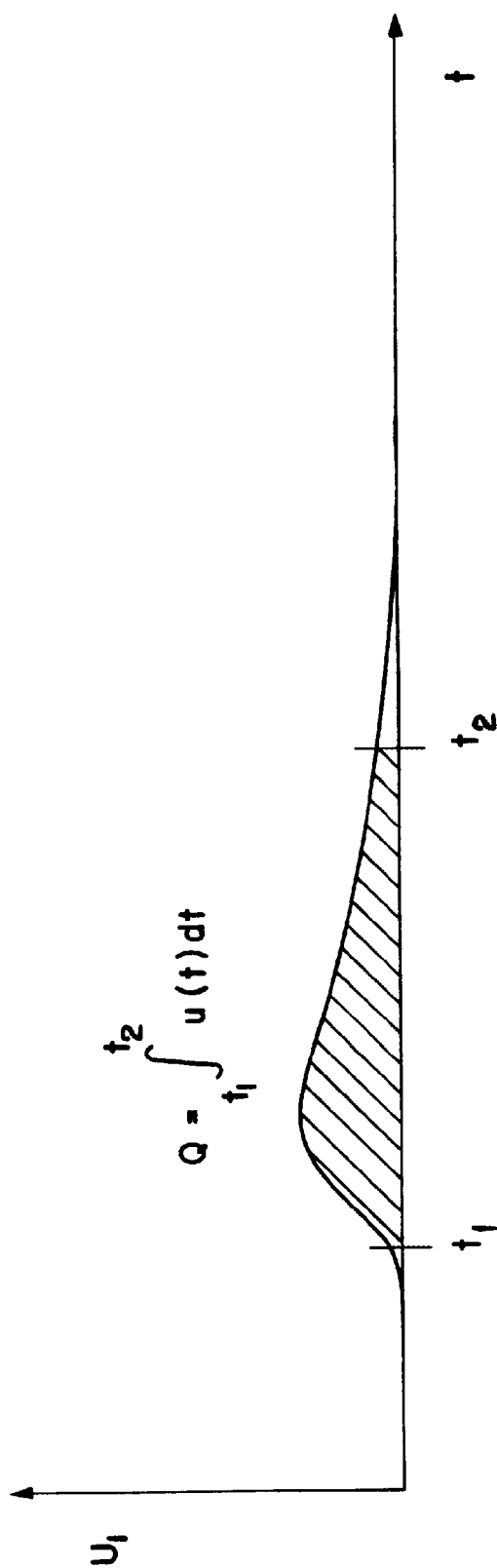
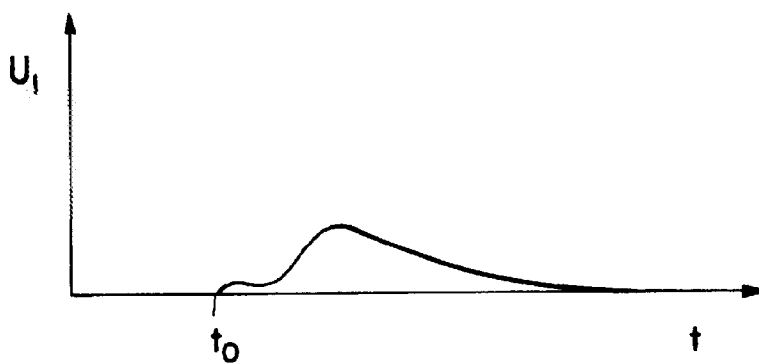
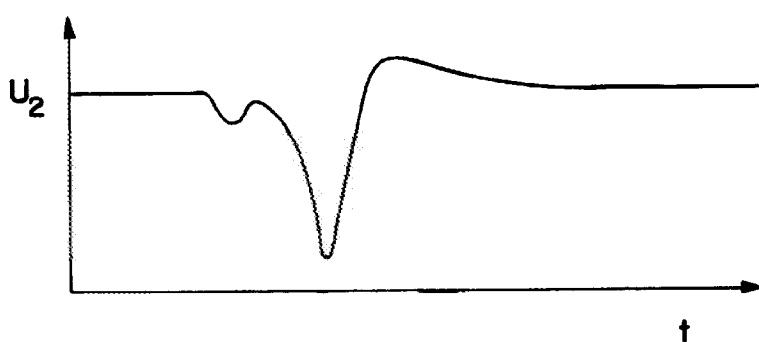
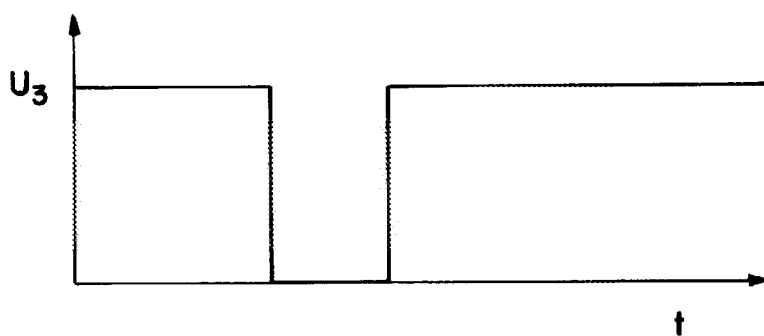
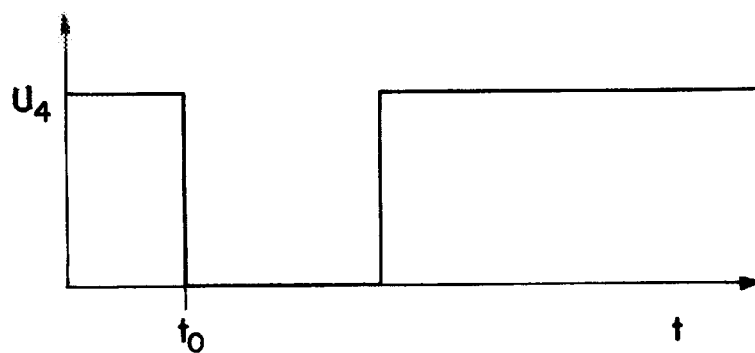


Fig. 6

*Fig. 7(a)**Fig. 7(b)**Fig. 7(c)**Fig. 7(d)*

AEROSOL INHALER

The invention relates to an aerosol inhaler for a medicinal substance to be inhaled and to an electronic module for use in association with such an inhaler.

An aerosol inhaler is to be understood as a device with the aid of which a patient can actively breathe in a given dose of a medicinal substance to be inhaled. A typical application for such a device is an acute asthma attack. Upon the actuation of a corresponding actuating element, the aerosol, consisting of a propellant and of the medicinal substance present in said propellant and distributed therein, passes from the supply container provided therefor, through a nozzle, into the air channel of a mouthpiece from where it is actively inhaled by the patient. The aerosol emission and atomization can be triggered electronically or mechanically.

Previously it was not possible to detect whether, upon the actuation of the actuating element, atomization had actually taken place or not. For example, this can be prevented by obstruction of the nozzle. Naturally atomization also does not take place when the aerosol supply container is empty. This can lead to complications as the patient has supposedly inhaled the medicine necessary to combat an acute attack, whereas in fact this is not true or only partially true. An only partial supply of the given dose frequently gives rise to a desire on the part of the patient to augment the effect of the medicinal substance by further inhalation. This can lead to a dangerous situation as a result of overdosing. Furthermore, the doctor caring for the patient loses an overview of the number of doses administered within a predetermined time interval, which is an impediment to responsible medical treatment.

Therefore, with this background, the object of the present invention is to further develop an aerosol inhaler of the type defined in such manner that it is at least possible to reliably recognise and evaluate the atomization of the aerosol upon the actuation of the actuating element. In accordance with further aspects of the invention, a series of evaluations relating to some treatment parameters, such as the number of administered doses, the doses remaining in the supply container and the indication thereof, as well as for example the checking of the aerosol to determine whether it corresponds to the doctor's prescription, are to be possible. Furthermore, an electronic module is to be provided for use in association with such an inhaler, which electronic module fulfils the electronic part of the object of the invention but in principle can also be used in the case of all known aerosol inhalers, and thus as an accessory to an aerosol inhaler.

In accordance with the invention, it is thus provided that the inhaler be equipped with an electronic module which comprises an evaluating electronic unit for function monitoring which is supplied with signals from at least one thermal sensor arranged in the flow region of the nozzle and from a device for recognising the actuation of the actuating element, and comprises a display device for the output of the evaluation result produced by the evaluating electronic unit.

The crux of the invention thus consists in that a thermal sensor is arranged directly on the nozzle in which the atomization of the aerosol takes place. This permits a positive detection of the atomization of the aerosol on the basis of the recognition of the actuation and of the cooling of the propellant which occurs upon atomization, in that the cooling of the propellant leads to the cooling of the thermal sensor and a clearly defined electric signal can be generated. Malfunctions, such as obstructed nozzles or an empty aerosol supply container, can thus be reliably detected.

In a special and simple exemplary embodiment, the evaluating electronic unit generates a warning signal when

atomization does not take place, and a signal representing the number of inhalation doses still contained in the supply container. These signals are communicated to the patient by means of a suitable display or, in the case of the warning, with an acoustic signal. As a result of the monitoring of the atomization the user can be warned when no atomization has occurred and thus he has not inhaled any medicinal substance, as can happen when a supply container is empty or also in particular when a nozzle is obstructed.

In accordance with a further advantageous development, it is provided that the thermal sensor detects the air flowing past it at the start of the inhalation, generates a corresponding signal therefrom, and sends this signal to the evaluating electronic unit which itself generates a signal which is optically and/or acoustically displayed as a coordination aid for the patient in the inhalation process.

The background to this further development is as follows:

The correct inhalation of the aerosol ideally proceeds in such manner that, having exhaled, the patient applies the device to his mouth and after the start of the inhalation triggers the atomization by depressing the actuating element. Many users have problems however in coordinating their breathing and the triggering of the atomization. An incorrect timing sequence of inhalation and triggering diminishes the effect of the medicament however, and impairs the clinical result. It is here that the described further development comes into effect in that immediately following the start of the inhalation the patient is informed by means of the optical or acoustic display that atomization is imminent. In this way the clinical result of the treatment is distinctly improved.

In accordance with a further embodiment it is provided that a further thermal sensor is arranged outside of the flow path of the aerosol, which further thermal sensor generates a reference signal which is likewise fed to the evaluating electronic unit and is linked with the signal from the first thermal sensor in such manner that the result permits the emitted quantity of aerosol to be deduced. The linking can take place, for example, in a differential amplifier in which it is possible to form the time characteristic of the difference between the temperature of the first thermal sensor arranged directly on the nozzle and the environmental temperature. The downstream, evaluating electronic unit then receives this difference signal and the integration of said signal within suitable limits supplies a value which, with the aid of a relation stored in a memory of the evaluating electronic unit, leads to the atomized quantity of aerosol. As a result of the quantitative detection, after each inhalation the patient can be given precise information as to whether a further inhalation is necessary. In the event of the undershooting of a specified quantity, preset in the program of the evaluating electronic unit, a warning signal can be generated which informs the patient that too little active ingredient has been inhaled. This monitoring possibility leads to greater reliability in the use of inhalers and to a more efficient therapy.

Alternatively, the emitted quantity of aerosol can be determined in that prior to the atomization the environmental temperature of the thermal sensor, which is anyhow arranged in the region of the nozzle, can be detected, digitalized and stored in the evaluating electronic unit. When the aerosol is now atomized during inhalation, the time characteristic of the temperature changes of the sensor is detected as so-called temperature profile. This temperature profile is digitalized and the previously stored environmental temperature is subtracted therefrom. The integration of the difference within suitable limits supplies a value which, with the aid of a relation stored in the memory of the evaluating

electronic unit, leads to the atomized quantity of aerosol. The relation between the output voltage of the sensor signal amplifier and the temperature of the sensor can be stored in the memory of the evaluating electronic unit. Any non-linearities of the sensor and the signal amplifier, and thus also the influence of shifts in operating point, caused by changes in the environmental temperature, can be computationally eliminated in the evaluating electronic unit.

If, in accordance with a further embodiment, the evaluating electronic unit comprises a microcontroller, the latter is preferably assigned a memory for the storage of data as well as a serial interface for communication with an external computer.

This embodiment provides the doctor in charge with the possibility, entirely novel in the relevant field, of monitoring whether the patient has actually inhaled the number of inhalation doses prescribed by him, and the time interval within which this has taken place. An abundance of data to be input into the memory, and functions associated therewith, are possible. Thus for example the doctor can also predetermine a time interval after which a further inhalation is to take place, and by means of a real-time clock present in the module an optical and/or acoustic signal is generated to remind the patient of the further inhalation.

The functions can be monitored and the implementation or non-implementation thereof can likewise be stored in the memory. On the occasion of a further visit to the doctor in charge, this data can then be read out via the serial interface and interpreted by the doctor. For the input into and output from the memory, the electronic module is to be connected via the serial interface—as already mentioned—to an external computer.

The presence of the evaluating electronic unit in the inhaler according to the invention facilitates further functions; in accordance with another embodiment the aerosol supply container can consist of a replaceable part so that it is detachably insertable into the inhaler. The exterior of the detachable supply container can have optically coded surfaces, such as are known for example in connection with the so-called DX-coding of miniature film cartridges in photography. The evaluating electronic unit is then designed in such manner that it can decode the information contained in this code. This information can for example indicate the type of active ingredient of the medicinal substance in the aerosol and the expiry date thereof. This data can be read out and compared in the microcontroller of the evaluating electronic unit for example with the information relating to the type of active ingredient input by the doctor. In the event of differences, an alarm signal can be triggered. The aforementioned real-time clock in the electronic module can be used to check the expiry data of the medicinal substance in the aerosol and to trigger an alarm when the expiry date is exceeded.

In this embodiment the replaceable supply container can also itself comprise an electronic memory; the data stored in this memory can be read out by the evaluating electronic unit and the evaluating electronic unit can input data into this memory. This memory can be provided in addition to the aforesaid optical coding or also by itself. For the data exchange between the inhaler and an external computer located, for example, at the doctor's premises, a plug-in EEPROM module which retains its data without a power supply can be used. The external computer has an adapter via which data can be input into the EEPROM module and also read out from the latter. Via this storage module, on the one hand the information concerning the type of active ingredient and the prescribed treatment can be communi-

cated to the device and on the other hand the device itself inputs the therapy actual data therein.

In another embodiment a sensor contact can be arranged on the mouthpiece of the inhaler. The signal from this sensor contact is fed to the evaluating electronic unit. It is thus possible to check whether, in the case of correct atomization, the patient has actually received the medicinal substance. This ensures that an atomization which, although correct, has been released into space and thus has not reached the patient, is not recorded in the memory as an administered dose.

Here it should again be emphasised that all the aforementioned monitoring possibilities are conditional upon the inhaler being provided with a thermal sensor directly on the nozzle where the aerosol is atomized, and with a device for recognising the actuation of the actuating element and with an evaluating electronic unit which evaluates the signals from this sensor and from the actuation-recognition device. The electronic module referred to in the introduction, as a part which is to be handled independently of the actual inhaler and which can itself constitute a commercial article, is provided in accordance with the invention with a separate housing which can be detachably secured to the inhaler and comprises, projecting away from itself, the at least one thermal sensor which is to be arranged in the direct vicinity of the nozzle opening in the inhaler.

The electronic module can be produced and tested independently of the inhaler. Only in the last production step is the electronic module clipped onto the device and the complete device subjected to final testing. However, it can also be marketed separately, independently of a concrete type of inhaler and serve as accessory.

In accordance with an advantageous further development the aforementioned second thermal reference sensor is also arranged on the electronic module, whereby the unit as a whole becomes very compact as this second sensor is not to be applied, for example, to the inhaler, which indeed would additionally require the establishment of an electric connection.

The thermal sensor or sensors is/are preferably NTC resistors, thermistors or surface thermoelements, i.e. elements whose electrical properties change in an evaluable manner in the event of a change in temperature.

The evaluating electronic unit can be formed by a microcontroller or a customised circuit in which all the necessary electronic functions are integrated. This design allows a reduction in the space required for the evaluating electronic unit and the power requirement and—due to the associated reduction in the battery volume—in the overall volume of the electronic module. The circuit board of the electronic module advantageously can be constructed in accordance with SMD technology. For reasons of space and costs the microcontroller can be assembled without the use of an IC housing in accordance with chip-on-board (COB)—or tape-automated-bonding (TAB) technology. The display unit and necessary batteries are fixed on the circuit board via a clip-on plastics frame and electrically connected to the circuit board via conductive rubber and contact springs.

The switching on and off of the device can take place without an additional operating step by the removal and application of the inhaler cap. If the cap remains open for a relatively long time interval, after a specified time the electronic unit is automatically switched to a so-called "sleep mode" and is automatically "awoken" by the triggering of an inhalation. When the cap is in place, mechanical locking can be provided which prevents the triggering of the atomization.

The display unit can preferably consist of a LCD with a 3-digit, 7-segment display and a symbol for the daily dose warning, battery warning and display of a device fault.

When a newly filled aerosol supply container is inserted in the inhaler, it is necessary to actuate a reset pushbutton on the electronic module whereby the remaining dose is set at a value corresponding to a full container. This function can also be implemented, in accordance with another embodiment, by means of the actuation-recognition device which sends a signal to the evaluating electronic unit both when the actuating element is activated and when the container is changed. The reset pushbutton is then not required.

The inhalation process of the inhaler according to the invention can also be electronically triggered. The electronic unit required for this purpose can likewise be accommodated in the electronic module. Incorrect triggerings are substantially prevented by a sensor contact on the mouthpiece.

The electronic recognition of the inhalation phase, referred to in the foregoing, by means of the thermal sensor in the flow region of the nozzle can also be used to trigger the atomization fully automatically via the breath. For this purpose, after a corresponding signal evaluation, the evaluating electronic unit sends a signal to the actuating element of the inhaler and thus triggers the atomization. The coordination is then assumed in full by the device. The patient need only apply the device to his mouth and inhale.

The evaluation of the sensor signal can also take place in that, after amplification, the analogue signals are immediately digitalized, the function of the above described comparators is assumed by the program of the evaluating electronic unit, and the corresponding switching levels and delay times are determined by the program.

In the following the inhaler according to the invention will be explained in detail in the form of an exemplary embodiment. In the drawings:

FIG. 1 is a front view of the inhaler with electronic module clipped-on laterally;

FIG. 2 is a side view of the inhaler according to FIG. 1;

FIG. 3 is a plan view of the device according to FIGS. 1 and 2;

FIG. 4 is a principal circuit diagram of the evaluating electronic unit;

FIGS. 5a to 5c show time characteristics of output signals and

FIG. 6 shows a time characteristic of the integration of the difference signal between the thermal sensor at the nozzle opening and the reference sensor, and

FIG. 7 illustrates further time characteristics of output signals in the case of which the inhalation phase is electronically evaluated.

FIGS. 1 to 3 are views of the inhaler according to the invention which represent only principal diagrams and do not correspond to actual sectional illustrations.

The inhaler 1 according to the invention comprises a supply container 2 for an aerosol. In the present case the supply container 2 is detachably connected to a housing which has a mouthpiece 6 with air channel 7 extending therein. By means of an actuating element (not shown here) a dose of the aerosol is inlet from the supply container 2 into the nozzle 4 where it is atomized. The patient breathes in this atomized aerosol through the air channel 7.

During this process the supply container 2 moves and via the actuation-recognition device 8 releases a signal which is fed to the evaluating electronic unit 31. The first thermal sensor 5 is arranged directly at the opening of the nozzle 4. When an atomization from the nozzle 4 takes place, the

propellant expands and the temperature in the region of the nozzle opening falls. This fall in temperature is detected by the thermal sensor 5, which latter generates a corresponding signal which is likewise fed to the evaluating electronic unit 31.

As already mentioned, in the present case the electronic module 3 is clipped onto the inhaler 1 and can be handled independently. It is of compact construction and contains all the necessary components, of which the batteries 36 and the optical display unit 34 have been provided with reference symbols in FIGS. 1 to 3. The optical display unit preferably consists of a 3-digit, 7-segment LCD display. The principal circuit diagram of the evaluating electronic unit 30 is shown in FIG. 4.

In the present case the main component is an evaluating electronic unit 31 which is supplied with the signal from the actuation-recognition device 8 and the signal from the thermal sensor 5. The evaluating electronic unit is not activated until the contact 33 is closed, which occurs when the cap of the device has been removed.

The circuit is supplied by the battery 36. In the present case the display takes place via the aforementioned display unit 34.

Finally a reset switch 35 is also provided, which must be actuated when a newly filled supply container is inserted into the inhaler 1 so that the remaining dose is set, in the memory of the evaluating electronic unit 31, at a value corresponding to a full supply container.

The signal processing will be briefly explained with reference to FIGS. 5 and 6.

FIG. 5a illustrates the curve of the voltage U_1 across the thermal sensor 5. Upon the expansion of the propellant in the nozzle 4 and the accompanying cooling of the sensor 5, the voltage U_1 initially rises steeply and after the atomization process falls to its original value in accordance with the thermal time constant.

FIG. 5b shows the time characteristic of an output voltage U_2 of a frequency-selective amplifier, to the input of which the voltage U_1 from FIG. 5a is applied. It can be seen that U_2 has a pronounced pulse in the case of atomization (event).

The voltage U_2 is fed for example to a comparator which in the rest state has a constant positive output voltage and in the case of correct atomization emits a negative pulse and at the time of an event temporarily assumes the voltage zero. The voltage U_3 is the digital input signal for the evaluating electronic unit. Amplifier and comparator can form part of the evaluating electronic unit.

Finally FIG. 6 shows the possibilities of electronic evaluation when a further thermal sensor (not shown) is provided as reference sensor which is exposed to the environmental temperature. Thus with the aid of a differential amplifier it is possible to form the time characteristic of the difference between the environmental temperature and the temperature of the nozzle 4 in the inhaler 1 and to supply this time characteristic to an analogue-digital converter of a processor contained in the microcontroller. The integration of this signal U_1 from FIG. 6 within suitable limits t_1 and t_2 supplies a variable

$$Q' = \int_{t_1}^{t_2} u_1(t) dt$$

which, with the aid of a clearly defined relation stored in a ROM storage module of the processor, leads to the actually atomized quantity of aerosol Q .

Finally FIG. 7 shows the signal processing in the event that, in accordance with a further development, the recognition of the inhalation phase is electronically evaluated.

The frequency-selective amplifier provided for the atomization recognition is preferably used for the signal processing.

FIG. 7a shows the time characteristic of the voltage U_1 across the thermal sensor, FIG. 7b shows the characteristic of the voltage U_2 at the output of the selective amplifier, FIG. 7c shows the characteristic of the voltage U_3 at the output of the comparator for the atomization recognition and FIG. 7d shows the time characteristic of the voltage U_4 at the output of a further comparator for the duration of a breathing-in and inhalation phase with correct atomization.

The voltage U_1 across the thermal sensor firstly has a small pulse, the front flank of which represents the start of the inhalation, i.e. when the first inhalation air passes the thermal sensor 5. The output voltage U_2 of the frequency-selective amplifier here already has an extremely marked pulse however. The voltage is fed to a comparator whose output voltage U_3 is the digital input signal for the evaluating electronic unit 31. The front flank of the voltage U_4 coincides with the start of the inhalation (t_0). After a delay time, freely defined in the program of the evaluating electronic unit 31, for this flank, the evaluating electronic unit 31 emits an acoustic signal via an electromechanical transducer (for example a piezoelectric oscillator).

The continued course of the voltage U_1 , namely in a more strongly positive ascent, and of the voltage U_2 with the strongly negative pulse result from the cooling of the thermal sensor 5 due to the correct atomization of the aerosol which follows the triggering. The output voltage U_3 of the corresponding comparator then has a negative pulse which is fed to the evaluating electronic unit.

For the patient, handling is simplified in that he starts to inhale having applied the inhaler to his mouth, and not until he hears a signal does he trigger the atomization by actuating the actuating element. This ensures that the patient does not trigger the atomization for example immediately after having applied the inhaler to his mouth and then inhale, or does not trigger the atomization when the inhalation phase is over, but triggers the atomization correctly with the inhalation. This serves to favourably influence the effects of the medicament.

The invention is not limited to the concrete exemplary embodiment explained here but includes all the possibilities, described in the foregoing, relating to the use and evaluation of the detected data.

What is claimed is:

1. An improvement in an inhaler for the administration by inhalation of an aerosol consisting of a medicament and a propellant, said inhaler being of a known design comprising:

- a) a supply container having propellant and medicament therein;

- b) a nozzle for atomizing propellant and medicament conveyed thereto, to form an aerosol therefrom, having an opening from which the aerosol so formed is expelled;

- c) means for conveying propellant from the supply container to the nozzle;

- d) an actuating element for causing the conveyance of propellant and medicament from the supply container to the nozzle, upon actuation by a user of the inhaler; and,

- e) a mouthpiece having a channel, through which the aerosol formed by the nozzle is expelled from the inhaler, so that it may be inhaled;

wherein the improvement comprises the addition of an electronic means for sensing and reporting whether aerosol has been expelled from the inhaler upon actuation by the user, said electronic means comprising:

- f) a first thermal sensor, located in the vicinity of the nozzle opening, which produces an electrical signal that varies in response to the temperature in the vicinity of the nozzle opening, including any decrease in temperature caused by the expulsion of aerosol from the nozzle opening;

- g) a second thermal sensor, located away from the vicinity of the nozzle opening, for developing a reference signal which represents the ambient temperature and which is not influenced by the expulsion of aerosol from the nozzle opening;

- h) an actuation-recognition device for producing an electrical signal upon actuation of the actuating means;

- i) an evaluating electronic unit, connected to the first thermal sensor, the second thermal sensor and the actuation recognition device, which evaluating electronic unit compares the signals of the two thermal sensors in order to determine whether there has been a decrease in temperature in the vicinity of the nozzle opening, and which uses the signal from the actuation recognition device to evaluate whether a decrease in temperature in the vicinity of the nozzle opening has coincided with actuation of the actuating means, and which thereby determines whether aerosol has been expelled from the inhaler upon actuation by the user; and,

- j) an electronic display, by means of which the determination of the evaluating electronic unit is reported.

* * * * *

Electronic Patent Application Fee Transmittal				
Application Number:		14925968		
Filing Date:		28-Oct-2015		
Title of Invention:		NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		
First Named Inventor/Applicant Name:		Adam BOWEN		
Filer:		Richard Douglas Shoop/Brian Flick		
Attorney Docket Number:		13211-713.303		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
Total in USD (\$)				180

Electronic Acknowledgement Receipt

EFS ID:	26075293
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	15-JUN-2016
Filing Date:	28-OCT-2015
Time Stamp:	15:56:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$ 180
RAM confirmation Number	2820
Deposit Account	504050
Authorized User	SHOOP, RICHARD D

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_6-15-2016.pdf	272546	yes	4
			7e9a162af5aa29b2260b3d40190f940541ad5464		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Transmittal Letter		1	3	
	Information Disclosure Statement (IDS) Form (SB08)		4	4	
Warnings:					
Information:					
2	Foreign Reference	JP10-501999AwEngEquiv.pdf	3881257	no	32
			9f5f4be56c683c9397af0c0f9f521e95b21f35e6		
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30802	no	2
			38ee338e6843acce2e3e83608cea6f7251c71d1c		
Warnings:					
Information:					
Total Files Size (in bytes):			4184605		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8

I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on 6-15-2016.

Brian Flick
Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
First Named Inventor : Adam Bowen
Filed : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
AND METHODS THEREOF
Customer No. : 66854

**INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98**

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and /or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT

☐ **37 CFR §1.97(b)**

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ 1). Within 3 months of the application filing date, or
- ☐ 2). Within 3 months of entry of a national stage as set forth in § 1.491, or
- ☐ 3). Before the mail date of a first Office Action on the merits, or
 - ☐ 3a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
- ☐ 4). Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
 - ☐ 4a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☐ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☐ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☐ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☐ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☒ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under § 1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

- A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement
- AND--
- B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☐ **37 CFR §1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☐ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☐ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☐ **37 CFR §1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ 3). A copy of each application specification is not submitted because the application is stored in the IFW. Cite no(s):

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☐ **37 CFR §1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☐ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

- ☐ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**
- ☐ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☒ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**
- ☒ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☒ 2a). An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): 585 **--AND/OR--**
- ☒ 2b). A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): 585 **--OR--**
- ☐ 3). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

STATEMENT UNDER 37 CFR § 1.97(e)

- ☒ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. Cite no(s): 585
- ☐ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement. Cite no(s):

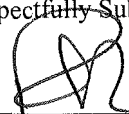
STATEMENT UNDER 37 CFR § 1.704(d)

- ☒ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

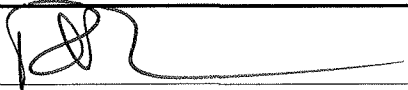
- ☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$180.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

By: 
Richard D. Shoop, Reg. No. 45,763

Dated: June 15, 2016

Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0		
Practitioner Docket No.: 13211-713.303	Application No.: 14/925,968	Filing Date: October 28, 2015
First Named Inventor: Adam BOWEN	Title: NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF	
<p>APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.</p> <ol style="list-style-type: none"> 1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (e.g., a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c). 2. The above-identified application contains an outstanding final rejection. 3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect. 4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection. 5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response. 6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web). 7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, e.g., extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.] 8. By filing this certification and request, applicant acknowledges the following: <ul style="list-style-type: none"> • Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0. • The examiner will verify that the AFCP 2.0 submission is compliant, i.e., that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions: <ul style="list-style-type: none"> ○ The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, e.g., by mailing an advisory action. ○ If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview. <ul style="list-style-type: none"> ▪ The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate. ▪ If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116. 		
Signature 	Date June 15, 2016	
Name (Print/Typed) Richard D. Shoop	Practitioner Registration No. 45,763	
<p>Note: This form must be signed in accordance with 37 CFR 1.133. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.</p>		
<p>☐ * Total of _____ forms are submitted.</p>		

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8	
I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on June 15, 2016.	
/Mary Buggie/	6/15/2016
Mary Buggie	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
First Named Inventor: : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL
DEVICES AND METHODS THEREOF
Customer No. : 66854

AMENDMENT AND RESPONSE UNDER 37 C.F.R. § 1.116

This communication is in response to the final Office Action dated May 13, 2016, for which a response is due August 13, 2016. Thus, this response is timely filed. Applicants submit herewith a Certification and Request for Consideration Under the After Final Consideration Pilot Program (2.0) in order for the Examiner to fully consider the amendments made herein. Finally, a Declaration Under 37 C.F.R. § 1.132 providing support and evidence of commercial success is also submitted herewith.

The Commissioner is authorized to charge any fees to make this filing timely to Deposit Account No. 50-4050.

Amendments to the Claims are shown in the listing of claims that begins on page 2.

Remarks/Arguments begin on page 6 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick, wherein:
 - a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and
 - c. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from the fluid storage compartment to the heating element and heating at least a portion of the nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C;
wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL on average, and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
2. (Currently amended) The method of claim 1, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between about 1:1 and 1:3.
3. (Original) The method of claim 1, wherein the nicotine formulation further comprises at least one flavorant.
4. (Original) The method of claim 1, wherein the nicotine concentration is about 4.5%.
5. (Cancelled)

6. (Original) The method of claim 1, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
7. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick, wherein:
- a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the nicotine formulation comprises protonated nicotine;
 - c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol;
 - d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the low-temperature vaporizer; and
 - e. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from the fluid storage compartment to the heating element and heating at least a portion of the nicotine formulation between about 100°C and 300°C to generate an inhalable aerosol;
- wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
8. (Currently amended) The method of claim 7, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
9. (Original) The method of claim 7, wherein the nicotine formulation further comprises at least one flavorant.
10. (Original) The method of claim 7, wherein the nicotine concentration is about 4.5%.

11. (Cancelled)
12. (Original) The method of claim 7, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
13. (Currently amended) A low-temperature vaporizer, comprising:
a liquid reservoir;
a nicotine formulation within the liquid reservoir, the nicotine formulation comprising:
nicotine lactate;
propylene glycol; and
90%-30% vegetable glycerol;
wherein a concentration of nicotine in the nicotine formulation is from about 0.5% (w/w) to about 20% (w/w);
a vaporizing component configured to produce an aerosol from the nicotine formulation by heating at least a portion of the nicotine formulation between 100°C and 300°C,
wherein the liquid reservoir is connected to the vaporizing component by a wick; and
a mouthpiece configured to connect to the reservoir for inhalation of the aerosol;
wherein inhalation of the aerosol into the user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 min to about 8 min and a Cmax of over 10 ng/mL on average, and further
wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
14. (Original) The electronic cigarette of claim 13, further comprises a battery configured to provide power to the vaporizing component.
15. (Currently amended) The electronic cigarette of claim 13, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
16. (Original) The electronic cigarette of claim 13, wherein the nicotine formulation further comprises at least one flavorant.

Response dated: June 15, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

17. (Original) The electronic cigarette of claim 13, wherein the vaporizing component comprises a heating element in fluid communication with the nicotine formulation.
18. (Original) The electronic cigarette of claim 13, wherein the nicotine concentration is about 4.5%.
19. (Cancelled)
20. (Original) The electronic cigarette of claim 13, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.

REMARKS

Claims 1-4, 6-10, 12-18 and 20 were pending in this application. By this response, claims 1, 2, 7, 8, 13 and 15 have been amended. No new claims have been added, and no claims have been cancelled. The amendments to the claims and the new claims are supported throughout the specification, and particularly:

- (a) Support for the amendments to claims 1 and 7, reciting: “a nicotine formulation... within a fluid storage compartment,” may be found at least in paragraphs [0040]-[0066] (e.g., “[p]rovided herein is a cartridge in an electronic cigarette comprising a fluid storage compartment, wherein the fluid storage compartment stores a nicotine salt liquid formulation...”).
- (b) Support for the amendments to claims 1 and 7 reciting: “...connected to a heating element by a wick” may be found at least in paragraphs [0640]-[0642] (e.g., “heater comprises a heater chamber, a fluid wick, and a resistive heating element in contact with the fluid wick”). One of skill in the art would understand, based on at least this disclosure, that the inventors had adequately described the recited use of a wick connecting the liquid nicotine formulation to the heater (heating element).
- (c) Support for the amendments to claims 1 and 7 reciting: “wicking the nicotine formulation from the fluid storage compartment to the heating element” may be found at least in paragraphs [0640]-[0642], as mentioned above describing devices in which the fluid storage compartment is in fluid communication with a heater (heating element) (see [0030]-[0031] (“...a heating element in fluid communication with the nicotine salt liquid formulation... a fluid storage compartment that stores the nicotine salt liquid formulation”), wherein the connection to the heater is a wick (see, e.g., paragraph [0642], “heater comprises a heater chamber, a fluid wick, and a resistive heating element in contact with the fluid wick”). One of skill in the art would understand, based on at least this disclosure, that the inventors had described the recited wicking of nicotine, using the wick, from the fluid storage compartment to the heater (heating element).

(d) Support for the amendment to claims 1 and 13 to recite that “wherein inhalation of the aerosol into a user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in ... a Cmax of over 10 ng/mL on average” may be found at least in paragraph [0290].

(e) Support for the amendment to claim 13, reciting “wherein the liquid reservoir is connected to the vaporizing component by a wick” may be found at least in paragraph [0642], “heater comprises a heater chamber, a fluid wick, and a resistive heating element in contact with the fluid wick”). One of skill in the art would understand, based on at least this disclosure, that the inventors had described the recited connection between the liquid reservoir and the vaporizer (e.g., heater).

Thus, no new matter has been added. Amendment of the claims is not to be considered a dedication to the public of any subject matter.

Thus, claims 1-4, 6-10, 12-18 and 20 are currently under consideration. Reconsideration of these claims is requested in view of the amendments and the following remarks.

INFORMATION DISCLOSURE STATEMENT

Applicant notes that a Supplemental Information Disclosure Statement was filed 5/12/2016. A Supplemental Information Disclosure Statement is also filed herewith. It is respectfully requested that these Supplemental Information Disclosure Statements be considered and the PTO Forms 1449/SB08 be initialed and returned with the next Action.

CLAIM REJECTIONS UNDER 35 U.S.C. § 112

Claims 2, 8 and 15

Claims 2, 8 and 15 currently stand rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Response dated: June 15, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

By this response, Applicants have amended claims 2, 8 and 15 to fully address the objections mentioned above (e.g., by amending “organic acid” to “lactic acid”). Thus, this rejection has been fully addressed and rendered moot.

DOUBLE PATENTING

Claims 1-4, 6-10 and 12

Claims 1-4, 6-10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 9,215,895 to Bowen et al. (“Bowen ‘895”) in view of U.S. Patent Application Publication No. 2013/0255702 to Griffith, Jr. et al. (“Griffith”).

The Applicants respectfully disagree.

By this response, independent claims 1, 7 and 13 have been amended, emphasizing the lack of obvious subject matter between pending claims 1-4, 6-10 and 12 and the cited Griffith references. Should the Examiner maintain the nonstatutory double patenting rejection but otherwise indicate the claims are allowable, the Applicants with favorably consider filing a terminal disclaimer to overcome this rejection; filing such a terminal disclaimer earlier would be premature.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-4, 6-10, 12-18 and 20

Claims 1-4, 6-10, 12-18 and 20 currently stand rejected under 35 U.S.C. § 103 as being unpatentable over Griffith as evidenced by www.e-cigarette-forum.com’s PG-VG-PEG Discussion Posting (“the PG-VG-PEG Internet Posting”) in view of U.S. Patent Application Publication No. 2014/0261474 to Gonda (“Gonda”) and U.S. Patent Application Publication No. 2009/0151717 to Bowen et al. (“Bowen ‘717”).

The Applicants respectfully disagree. The combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 does not suggest all of the features recited in the currently pending claims. Further, there is a substantial objective indicia of non-obviousness, as evidenced by the 37 C.F.R. § 1.132 Declaration by Dr. Gal Cohen submitted herewith, which provides significant evidence of commercial success that is attributable to the features recited in the Applicants' pending claims.

A. The combination of Griffith, the PG-VG-PEG Internet Posting, Gonda and Bowen does not suggest all of the features of claims 1-4, 6-10, 12-18 and 20

The combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 does not suggest all of the features recited in the claims. In particular, this combination of references does not suggest:

- (1) deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier *within a fluid storage compartment connected to a heating element by a wick;*
- (2) operation of the low-temperature vaporizer comprises *wicking the nicotine formulation from the fluid storage compartment to the heating element* and heating at least a portion of the nicotine formulation to generate an inhalable aerosol;
- (3) wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL on average.

Regarding the first and second elements, none of Griffith, PG-VG-PEG Internet Posting, Gonda or the Bowen '717, alone or in combination, suggests deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick or wicking the nicotine formulation from the fluid storage compartment to the heating element. Griffith teaches a solid-state device in which nicotine formulation, and particularly the vapor precursor material, is incorporated (e.g., coated on, absorbed by or adsorbed) in or on a carbonized substrate, so that they are "integral with the carbonized

substrate". See Griffith, paragraphs [0009], [0014], [0089], and [0122]. Griffith does not teach or suggest keeping the biological material within a fluid compartment and connecting to the heating element by a wick. Instead, Griffith suggests that the vapor precursor material is saturated onto the substrate that has been carbonized. It goes counter to Griffiths' teaching of the benefit of using a carbonized substrate to directly integrate with the vapor forming material to include an intervening wick. Griffith emphasizes the importance of the improved-resistivity of the carbonized substrate. It would not make sense to include an intermediate structure, such as a wick, between the vapor precursor material and the carbonized substrate of Griffith.

Similarly, none of PG-VG-PEG Internet Posting, Gonda and the Bowen '717 suggests deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick or wicking the nicotine formulation from the fluid storage compartment to the heating element. The PG-VG-PEG Internet Posting is silent as to this feature. Gonda describes devices and methods using solids (e.g., powdered material) or filtering a liquid through a membrane to form vapor. Finally, Bowen '717 teaches heating a viscous material in an oven.

In addition, the combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 does not suggest a method or apparatus in which inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma T_{max} from about 3 minutes to about 8 min, and a C_{max} of over 10 ng/mL on average.

As previously described, the Applicants' claims are directed a particular nicotine salt that results from combining a solution of nicotine (e.g., freebase nicotine) and lactic acid in a biologically acceptable liquid carrier including propylene glycol and 90%-30% vegetable glycerol. This nicotine salt formulation, when vaporized using a low-temperature vaporizer between about 100°C and 300°C, results in a user experience that closely mimics a traditional cigarettes; e.g., having a T_{max} that is between 3-8 minutes and a C_{max} greater than 10 ng/mL. The combination of nicotine and lactic acid in a carrier including propylene glycol and 90%-30%

vegetable glycerol for use in a low-temperature vaporization device operating between 100°C and 300°C is based, in part, on the Applicants' unique discovery that only certain nicotine salts (e.g., and therefore only certain organic acids forming these salts) have a nicotine C_{max} and T_{max} in blood plasma of a user inhaling the vapor that is similar to that of inhaling smoke from a traditional cigarette. For example, the Applicants' disclosure (see, e.g., figures 1-5 and accompanying description) describes for the first time the plasma T_{max} and C_{max} of a variety of nicotine formulations, and teaches which formulations (and specifically which nicotine salts) do and do not have this desired effect.

Without the Applicant's teachings, one of skill in the art would not be motivated to select the correct nicotine formulation and method of using it as described herein, and therefore it would not be obvious to combine references, including the Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 references raised by the Office Action. Specifically, without the Applicant's teaching, one of skill in the art would not know to select, from the universe of possible nicotine formulations, the proper nicotine, lactic acid and PG/VG carrier at the recited concentrations, and how to use this nicotine formulation to achieve the T_{max} of nicotine in the blood between 3-8 minutes (and a C_{max} of over 10 ng/mL).

The combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 does not suggest a method of using a low-temperature vaporizing device wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma T_{max} from about 3 minutes to about 8 min and a C_{max} of over 10 ng/mL on average. Further, it would not be obvious to modify the combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 to achieve the recited invention.

The final Office Action of May 13, 2016 argues that Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen '717 suggest a method of using a nicotine formulation that achieves a blood nicotine T_{max} of between 3-8 min (and a C_{max} of over 10 ng/mL), because this method would be obvious since "Gonda teaches that administering an aerosolized, liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to

effectuate a peak level of nicotine in the blood plasma after a very short period of time – mimicking that which is typically achieved during actual cigarette smoking – can be accomplished.”

Applicants respectfully disagree. A suggestion that a recited feature could be accomplished is not sufficient to show obviousness. Although Gonda mentions the Tmax of nicotine due to cigarettes (Gonda [092]), Gonda stops short of teaching that this was actually achieved. More importantly, although Gonda provides a long list of factors that may affect the rate of absorption (e.g., Tmax), including: amount or concentration of nicotine, pH, duration of particle generation, and particle size (see Gonda [0032], [0064] and [0099]), none of these variables are responsible for the Tmax and Cmax effect recited in the Applicant’s claims. As described in the Applicants’ specification, it is the unexpected combination of nicotine, lactic acid, and PG/VG in a liquid solution that is vaporized by heating between 100 and 300 °C and inhaled to provide a Tmax of between 3-8 min (and a Cmax over 10 ng/mL) as recited in the Applicant’s claims. While Gonda suggests that for some formulations could be tweaked by adjusting pH and/or particle size to modify their absorption, Gonda does not show the recited Tmax levels are actually achieved. This is because, as described in the Applicant’s disclosure, particle size and pH (and any of the other factors mentioned by Gonda) are not sufficient by themselves, to achieve the proper Tmax, particularly when wicking a liquid reservoir onto a heater that is heated between 100-300 °C to vaporize. Importantly this ability to achieve the target Tmax with a nicotine formulation is not dependent on mere pH, but surprisingly depends on the type of acid included in the formulation, which was not known in the art until the Applicant’s invention. The variables referenced by Gonda (e.g., nicotine concentration, pH, etc.) alone or in combination are not sufficient. As Applicants have described, the type of organic acid (including, in particular, lactic acid) is also critical.

Without this essential knowledge, or without the use of hindsight, it cannot be obvious to modify the Griffith reference to achieve the recited Tmax and Cmax values, even if Gonda suggests that it may be beneficial. Although the Office Action asserts that it would be routine for one of skill in the art, given the known “results oriented parameters” of Gonda (e.g., pH,

nicotine concentration, particle size) to modify Griffith to achieve the claimed Tmax features, since only “routine experimentation would be needed” to optimize these variables to achieve the “recognized result” (see, e.g., Office Action, page 10). Applicants disagree. The variables being ‘optimized’ in the instant claims are not the same as the variables identified as “results oriented” variables by Gonda. Instead, these variables are the liquid mixture, containing nicotine, the correct carrier mixture (PG/VG) and correct acid (e.g., lactic acid). In order to be obvious for optimization, a variable (or as here, a combination of variables) must be *recognized* as a results-effective variable in the prior art. See, e.g., *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In this case, none of these variables were recognized by the Gonda as relevant to the desired result (e.g., a Tmax of nicotine in the plasma between 3 and 8 minutes), and therefore it could not be obvious to optimize to achieve them. The “results oriented variables” cited by the Office Action in reference to Gonda (e.g., pH, particle size, nicotine concentration) are irrelevant if the wrong acid and therefore salt is generated (e.g., see paragraph [115] “... not all nicotine salts perform similarly to each other or to a traditional cigarette with respect to the rate of nicotine uptake in the blood at early time periods (0-1.5 minutes). These results are unexpected.”). Without knowing what variables must be optimized (e.g., which acid and therefore nicotine salt to use), it could not be obvious to optimize the combination Griffith and Gonda together or with any other reference.

Since the combination of Griffith, PG-VG-PEG Internet Posting, Gonda and the Bowen ‘717 does not suggest all of the features recited in claims 1-4, 6-10, 12-18 and 20, these claims cannot be obvious in light of these references.

B. Commercial Success of the Products attributable to the Claimed Features shows objective indicia of non-obviousness

The Supreme Court has recognized commercial success as a possible determinant of patent validity since 1876. *Smith v. Goodyear Dental Vulcanite Co.*, 93 U.S. 486, 495-96 (1876). In 1966, with the landmark decision of *Graham v. John Deere Co.*, the Court reaffirmed the vitality of secondary considerations “[a]s indicia of obviousness or nonobviousness.” (*Graham v. John Deere Co.*, 383 U.S. 1, 17-18). The Court listed commercial success as the first secondary

consideration. The commercial success of a product is highly probative of obviousness where the commercial success is attributable to the claimed features that are allegedly obvious; if a product commercially successful product was obvious to invent, then other competitors likely would have already developed it and the market for subsequent entrants to achieve commercial success would be depleted. The potential for achieving commercial success is thought to drive inventors to formulate solutions to existing problems to satisfy marketplace demands. Such evidence of commercial success may help prevent improper hindsight bias when comparing the claimed invention to a combination of prior art.

Applicants respectfully submit that the claimed invention, as supported by the attached declaration under 37 C.F.R. § 1.132, has had great commercial success directly resulting from the incorporation of the all of the features of the claimed invention.

Prior to the Applicants' invention, existing electronic cigarettes for delivering nicotine to a user did not include a nicotine formulation comprising nicotine, lactic acid, and a carrier of propylene glycol and 90%-30% vegetable glycerol that was vaporized so that inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min. A new vaporizer product incorporating all of the features recited in the Applicants' claims in the fall of 2015. In the eight months since its introduction, this product has exhibited nearly exponential sales growth. This commercial success is directly attributable to the features claimed by the Applicant's claims.

Attached hereto is a 37 C.F.R. § 1.132 Declaration by Dr. Gal Cohen. Dr. Cohen's declaration describes the NJOY Daily commercial electronic cigarette product, a low-temperature vaporizer (electronic cigarette). The NJOY Daily product incorporates all of the features recited in the claims. As established in Dr. Cohen's declaration and the associated exhibits, sales of the NJOY Daily product have grown rapidly since its introduction, eclipsing the sales of other electronic cigarettes, including other newly introduced and heavily advertised products that do not include the recited features. This commercial success is directly attributable to the claimed features, including in particular, the use of a nicotine mixture including lactic acid

and PG/VG, and the ability to achieve a Tmax within approximately the same time as a traditional cigarette (e.g., “wherein inhalation of the aerosol into a user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min”) and a Cmax of greater than 10 ng/mL.

(a) The NJOY Daily product includes all of the features recited in the claims

Paragraphs 7 and 8 of Dr. Cohen’s exhibit establish that the NJOY Daily electronic cigarette embodies all of the features recited in the claims. The NJOY product is an electronic cigarette including a liquid reservoir; a nicotine formulation within the liquid reservoir, in which the nicotine formulation includes: nicotine lactate (nicotine and lactic acid), and a carrier including propylene glycol and 90%-30% vegetable glycerol. The concentration of nicotine in the nicotine formulation is 4.5% (between 0.5% to about 20%) w/w. The fluid storage compartment is connected to a heating element by a wick. In operation, the NJOY Daily device produces an aerosol from the nicotine formulation by heating at least a portion of the nicotine formulation between 100°C and 300°C so that inhalation of the aerosol into a user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL. This is explicitly shown for the NJOY Daily product in Exhibit G (“Nicotine Delivery” graph).

(b) The NJOY Daily Product has Been Commercially Successful Because It Includes the Features Recited in the Applicants’ Claims.

The NJOY Product has enjoyed commercial success which has increased since its introduction into the market in the fall of 2015, as described by Dr. Cohen in detail in paragraphs 5 and 6. For evidence of commercial success to be probative of non-obviousness, there must be a nexus between the commercial success and the features recited in the claims. There are multiple lines of evidence showing that the commercial success of the NJOY Daily product is due (at least in part) to the feature recited in the claims. First, the NJOY Daily product has been specifically advertised as including the features recited in the claims, identifying these features key selling points to consumers. Second, consumer self-reporting data (testimonials) indicate that consumers are purchasing the NJOY daily product precisely because it includes the features

recited in the claims. Finally, the company selling the NJOY Daily device (NJOY Inc.) has itself stated that the recited features, in particular the Tmax properties (“nicotine absorption”) are at responsible for the commercial success. These points are all described in paragraphs 9-11 of Dr. Cohen’s declaration.

Although in many cases it may be difficult to attribute commercial success to particular recited features and not simply advertising (see, e.g., MPEP §716.03(B), citing *Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 227 USPQ 766 (Fed. Cir. 1985)), that is not the case here. Instead, advertisements for the NJOY Daily product explicitly touted the claimed features as selling points to the consumer. Thus, the success of this advertisement campaign itself hinged on the incorporation of the the recited features into the NJOY Daily product. See the Declaration of Dr. Gal Cohen, Exhibits F and G. As shown in electronic and print advertisements marketed to consumers and distributors, the NJOY Daily product was explicitly described as embodying the Applicants claimed features. For example, the NJOY Daily product was described as including nicotine solution including 4.5% nicotine, lactic acid, and 50/50 PG/VG that can provide “over 90%” of the satisfaction as a cigarette “during the first seven minutes,” based on a “clinical trial conducted by [an] independent lab measuring nicotine absorption in blood stream [Tmax]...”. Some advertisements went so far as to include a graph showing the Tmax and Cmax values for the NJOY Daily (compared to other products and a traditional cigarette) as shown by the flyer in Exhibit G.

The nexus between the recited features, including the nicotine solution with nicotine, lactic acid and PG/VG that results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL, is also shown by consumer testimonials (Exhibit H of Dr. Cohen’s declaration). Consumers have self-reported that they purchase and prefer the NJOY Daily product because of the recited features, compared to other commercial products that do not include these features. The rapid blood absorption (Tmax) is typically expressed by consumers as a nicotine satisfaction or “fix” similar or identical to traditional cigarettes.

Finally, as shown in Exhibit A of Dr. Cohen’s Declaration, the company offering the NJOY Daily product (NJOY, Inc.) directly attributes the commercial success to the rapid blood

Response dated: June 15, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

absorption (Tmax) (“NJOY attributes the Daily’s early success to the product’s accessible \$5.99 MSRP, as well as its ability to create a bridge to familiarity for adult smokers through its lightweight, soft touch design *and superior nicotine absorption.*”).

In light of this commercial success, which is directly attributable to the recited features of the Applicants’ claims, as evidenced by the attached 37 C.F.R. § 1.132 Declaration and as shown above, the Applicant’s respectfully request withdrawal of the 35 U.S.C. § 103 rejection of claims 1-4, 6-10, 12-18 and 20 and allowance of all of the currently pending claims.

Response dated: June 15, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

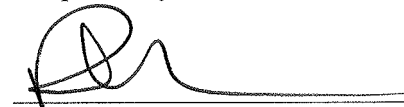
CONCLUSION

In light of the remarks set forth above, Applicants respectfully request the Examiner expedite the prosecution of this patent application to issuance. If it is determined that a telephone conference would aid in the prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 287-2164.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-4050** referencing docket no. 13211-713.303. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Date: June 15, 2016

Respectfully submitted,



Richard D. Shoop
Registration No. 45,763

SHAY GLENN LLP
2755 CAMPUS DRIVE, SUITE 210
SAN MATEO, CA 94403
TELEPHONE: 650.287.2164
FACSIMILE: 650.212.7562

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
Inventor(s) : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND
METHODS THEREOF
Customer No. : 66854

DECLARATION UNDER 37 C.F.R. § 1.132

I, Dr. Gal Cohen, declare as follows:

- (1) I hold a PhD in Molecular and Cellular Physiology from Stanford University.
- (2) I am the Head of Scientific and Regulatory Affairs at PAX Labs, Inc. ("PAX"), a market leader in vaporization (including electronic cigarette) technology, where I have been employed or affiliated since 2008.
- (3) PAX Labs is the applicant and owner of U.S. patent application no. 14/925,968, for which this declaration is being submitted.
- (4) As part of my employment at PAX, I monitor the sales and marketing of other electronic cigarette manufacturers, including NJOY, Inc.
- (5) In or around September of 2015, NJOY, Inc. released a new product, called the "NJOY Daily". Since its introduction, sales of the NJOY Daily product have grown substantially and the NJOY Daily has experienced a significant commercial success, particularly as compared to other electronic cigarettes. Exhibit A, attached hereto is a copy of an article from the June 10, 2016 edition of "Convenience Store Decisions." The article, dated March 30, 2016, is entitled "NJOY Daily E-Cig Sales Soar." As reported in the article, the NJOY Daily "is currently the fastest turning new e-vapor product, outselling other new products such as JTI's Logic Pro and Pax Labs' JUUL."
- (6) I have also monitored the sales of the NJOY Daily product using Information Resources, Inc. (IRI), a syndication service that tracks consumer product sales and marketing. IRI analysis of NJOY, Inc. shows that since its introduction, 4 week sales in all convenience store channels of NJOY Daily have grown from \$0 a year ago to just

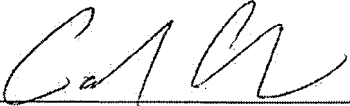
under a million dollars (\$908,604). In the same time period, sales of other, established NJOY, Inc., products (including “NJOY Vaping” and “NJOY Bold”) have decreased in sales by an aggregate of just over \$700,000. This data is shown in Exhibit B. NJOY, Inc. has included a graphic illustrating unit sales of the NJOY Daily product as part of its advertisement material promoting the product to distributors, which is shown in Exhibit C. The graphic shows the exponential growth of NJOY Daily sales based on IRI data using four week sales data for sales in all channels ending on January 3, 2016.

- (7) I have purchased and examined the NJOY Daily product. The NJOY Daily embodies all of the features of the pending claims of the U.S. patent application no. 14/925,968. The NJOY Daily is an electronic cigarette that includes a liquid nicotine formulation of nicotine, lactic acid, and a carrier of 50/50 propylene glycol (PG) and vegetable glycerin (VG). Exhibit D, attached hereto, is a description of the NJOY Daily product that is provided on the NJOY website (www.njoy.com/faq, last visited June 10, 2016). I have also requested and reviewed a chemical analysis of the liquid nicotine composition of a purchased NJOY Daily product, and have confirmed that the composition of this product is the same as recited in the claims of U.S. patent application no. 14/925,968. Specifically, the NJOY Daily nicotine formulation is a liquid solution of nicotine (between 46.8 and 47.3 mg/mL) and lactic acid (between 22.6 and 22.4 mg/mL) with a biologically acceptable liquid carrier of propylene glycol and glycerin (vegetable glycerol). The vegetable glycerol is between 90% and 30% of the liquid carrier. The chemical analysis was performed by a commercial chemical lab, Enthalpy Analytical, Inc., and a copy of this report is attached as Exhibit E. The liquid solution of the NJOY Daily product saturates a sponge that is held within a fluid storage compartment, and the liquid solution within the storage compartment is connected to a heating element by a wick. During operation of the NJOY Daily product, the nicotine formulation is wicked from the fluid storage compartment to the heating element and heated to between about 100°C and about 300°C to generate an inhalable aerosol.
- (8) The use of the NJOY Daily product also results in the nicotine plasma Tmax from about 3 min to about 8 minutes and a Cmax of over 10 ng/ml when the aerosol produced by the NJOY Daily is inhaled into the user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds. Exhibit G shows an example of advertising material promoting the NJOY Daily product which describes the product as “over 90 percent as satisfying as a cigarette during the first 7 minutes of use,” based on the Tmax and Cmax profile for the NJOY Daily. In Exhibit G, the statements referring to the increased satisfaction in strength and timing of the nicotine delivery refer to a clinical trial “conducted by [an] independent lab measuring nicotine absorption in [the] blood stream represented by mean of test subjects assessed on day 8 of use following 12 hours of abstinence.” Exhibit F shows two screen captures of the advertisement aimed at consumers for the NJOY Daily that describe the peak blood nicotine concentration (Tmax) occurring within the first seven minutes of use, which is describes as providing a satisfaction similar to what is achieved by a traditional cigarette. In addition, the Tmax and Cmax resulting from the NJOY Daily product is also described in advertising material targeting distributors, as shown in Exhibit G. Exhibit G is an advertising flyer distributed by NJOY Inc, targeting distributors and

customers of NJOY Daily. In Exhibit G, the graph titled “Nicotine Delivery” at the bottom right shows that the NJOY Daily has a Tmax between 3 minutes and 8 minutes, and a Cmax of greater than 10 ng/ml (mean nicotine concentration). The “Chart Notes” provided at the bottom of the flyer indicate that the graph represents a “[c]linical trial conducted by independent lab measuring nicotine absorption in blood stream represented by mean of test subjects assessed on day 8 of use following 12 hours of abstinence. N=18-20 per product. Subjects smokers aged 18-65 not currently attempting to quit. Products puffed (starting at time zero) every 30 seconds for 5 minutes.”

- (9) It is my opinion that the commercial success of the NJOY Daily product is attributed to the features recited in the claims of U.S. patent application no. 14/925,968. The Tmax and Cmax values of the NJOY Daily product which result from the nicotine solution including nicotine, lactic acid and the PG/VG carrier provide a cigarette-like satisfaction. The rapid onset (e.g., Tmax between 3 and 8 minutes) of a relatively high blood nicotine level (e.g., Cmax over 10 ng/mL) result in a user experience and satisfaction that is closer to the experience provided by a traditional cigarette. It has long been the goal of electronic cigarette manufactures to provide an electronic cigarette that can mimic the experience of a traditional cigarette, because of the potential for tremendous commercial success. There are numerous user-reported testimonials available online in which users discuss their reasons for purchasing the NJOY Daily product; the majority of such self-reporting comments refer to the cigarette-like experience that it provides.
- (10) In addition, the features recited in the claims, and particularly the Tmax and Cmax profiles, are used extensively in the NJOY Daily marketing and advertisement materials to drive consumer purchases. For example, the consumer advertisements show in Exhibit F tout the Cmax and Tmax properties as providing a user experience that is most similar to cigarettes. In Exhibit F, on the top left (“Meet NJOY Daily”), the advertisement claims that “over 90 percent as satisfying as a cigarette,” and on bottom of (“IT’S THAT SATISFYING”), a similar advertisement states “[o]ur latest innovation is now delivering the most authentic ‘smoking’ experience to date. We’re proud (and really freakin excited) to introduce the Daily – a labor of love that blends Satisfaction, Performance, Authenticity, Flavor and Design for an experience that’s more than 90% as satisfying as a cigarette during the first 7 minutes of use.” The advertisement of Exhibit G is even more explicit, graphically showing the Tmax and Cmax curves and describing the NJOY Daily as providing “[q]uick & strong satisfaction more like a cigarette”.
- (11) Finally, the NJOY company itself credits the nicotine absorption into the blood, the Tmax and Cmax properties of the NJOY Daily, as at least partially responsible for the commercial success. The recent article (“NJOY Daily E-Cig Sales Soar”) in Exhibit A cites NJOY as attributing the early success of the NJOY Daily product to “its lightweight, soft touch design and superior nicotine absorption.”
- (12) I declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further that these

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under the provisions of 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of any patent issuing upon U.S. Application Serial No. 14/632,161, or any continuing application thereof.

Signature: 
Gal A. Cohen, PhD

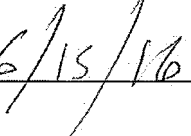
Date: 

EXHIBIT A

Convenience
Store
Decisions
June 10, 2016

TOP STORIESNEW PRODUCTS C-STORE TRENDSCHAIN OF THE YEARCATEGORY NEWS & DATA RACK PRICING

[Home](#) » [Recent CSD Articles](#) » [Categories](#) » [Today's News](#) » [NJOY Daily E-Cig Sales Soar](#)

NJOY Daily E-Cig Sales Soar

March 30, 2016 [CSD Staff](#) : [0 Comments](#)



Accessible pricing and lightweight, soft touch design help spur consumer demand for NJOY Daily.

E-cigarette manufacturer NJOY shared the latest IRI FDMxC ("All-Channel") data, revealing that the NJOY Daily disposable e-cig is currently the fastest-turning new e-vapor product, outselling other new products such as JTI's Logic Pro and Pax Labs' Juul.

The data indicates that NJOY Daily is finding a home in the hands of adult smokers looking for an introductory e-vapor product that delivers nicotine satisfaction more like a cigarette.

According to IRI data, NJOY Daily's 3 SKUs moved more than 37,000 units in the single week ending Feb. 21, 2016. This amounts to 23% greater unit sales per week when compared with Logic Pro and 281% greater unit sales per week than Juul.

NJOY attributes Daily's early success to the product's accessible \$5.99 MSRP, as well as its ability to create a bridge to familiarity for adult smokers through its lightweight, soft touch design and superior nicotine absorption. Thanks to their valued retail partners, NJOY has been able to leverage promotional support, merchandising, signage, and marketing assets to drive trial among adult smokers.

An early e-vapor pioneer, NJOY is currently the largest independent e-cigarette and vaping company in the USA. NJOY has heavily invested in R&D and market studies to further its ongoing commitment to product innovation based on consumer research and leading-edge science.

2436

EXHIBIT B
IRI Data

NJOY, Inc. sells 3 product lines:

- (1) NJOY vaping (vape pen and e-liquid bottles with a traditional nicotine formulation)
- (2) NJOY Bold (cigalikes with a traditional nicotine formulation)
- (3) NJOY Daily (cigalike with a lactic acid based formulation)

Based on data provided by Information Resources, Inc (IRI), in the past year, 4 week sales in all convenience store channels for all NJOY products have increased from \$2,079,734 to \$2,274,610. However, the proportion of sales represented by NJOY Daily has increased from 0% to 40%, while sales of all other products (NJOY vaping and NJOY Bold) have decreased by 60%.

	4 weeks ending 5/15/16		year ago		change y/y
vaping	\$879,301	39%	\$1,015,091	49%	(\$135,789)
Bold	\$486,705	21%	\$1,064,644	51%	(\$577,939)
Daily	\$908,604	40%	\$0	0%	\$908,604
Total	\$2,274,610		\$2,079,734		\$194,876

INTRODUCING NJOY[®] DAILY

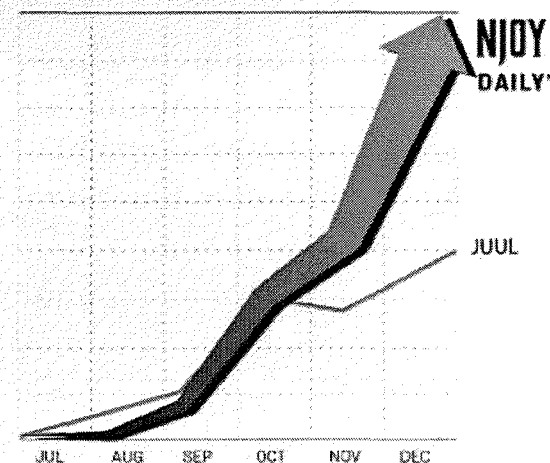
THE DIFFERENTIATED DISPOSABLE

DESIGNED WITH
RETAILERS IN MIND

REINVIGORATING CONSUMER TRIAL	<ul style="list-style-type: none"> • Everyday value – approximately 300 puffs for \$5.99 per stick • Quick & strong satisfaction more like a cigarette • Disposable lightweight stick
MAXIMIZE PURCHASE FREQUENCY & PROFITS	<ul style="list-style-type: none"> • ~40% margins* • 1 count configuration to maximize purchase frequency • Compact 5 count cartons for limited investment and optimal turns • Flavor freshness seal for extended shelf life • ~70% higher gross profit per week vs. leading rechargeable refills**
SELL THROUGH RATE SUPPORT	<ul style="list-style-type: none"> • Multi-million dollar consumer advertising campaign • Robust introductory price promotions • Modular merchandising displays and impactful signage • Trial generating activations • Targeted coupon delivery to adult smokers

**REINVIGORATING
CONSUMER TRIAL**
BY DELIVERING SATISFACTION
MORE LIKE A CIGARETTE.

IRI UNIT SALES
ALL CHANNEL***



Sources:

*Assumes average ABVP and cost = NJOY list price

**Assumes \$3.74 Gross Profit per leading rechargeable kit refill and assumes 7 units per week of consumption. "1 Unit" Definition: Disposable = 1 stick;

Recharge = 1 refillment. Assumes 1 unit purchased per store visit.

***IRI 4 Weeks Ending 12/31/14 All Channel = FDMx + C-Store

NJOY[®]
DAILY

EXHIBIT D

Screen captures from www.njoy.com/faq (taken 6/10/2016):

What is e-liquid?

The main ingredients by volume in NJOY's vape e-liquids are propylene glycol (PG) and vegetable glycerin (VG). The secondary ingredients are nicotine and flavors.

All of NJOY's e-liquids are made in the USA with domestic and imported ingredients, and contain pharmaceutical grade PG, VG and nicotine. The e-liquid in the following products also contain lactic acid: NJOY Daily (all flavors) and our Classic Tobacco and Menthol vaping e-liquids.

NJOY Vape e-liquids contain 50% vegetable glycerin (VG) and 50% propylene glycol (PG).

The VG/PG ratios in the Artist Collection:

Paramour: 50/50 Hedon's Bite: 60/40 Sacré Coeur: 50/50 Dragon Scape: 70/30 Samba Sun: 60/40

Daily, the disposable e-cig that offers the most authentic 'smoking' experience is available in Rich Tobacco, Cool Menthol, Blue + Black Berry and Classic Tobacco (online only...coming soon).

Kings, the disposable e-cig that started it all, comes in bold, gold and menthol flavors.

Recharge comes in a range of flavors beyond menthol and traditional, including vanilla bean and pomegranate.

NJOY Vaping e-liquids come in a wide variety of flavors. You can see the all here.

Artist Collection is an exclusive line of complex e-liquids crafted by five leading artists in the vape industry in partnership with NJOY.

Check out all of our flavor chambers and e-liquids today.

How much nicotine is in NJOY products?

Ask and you shall receive:

NJOY Daily

- Rich Tobacco: 4.5% nicotine by weight
- Cool Menthol: 4.5% nicotine by weight
- Blue + Black Berry: 4.5% nicotine by weight

Some of your products now list lactic acid in the ingredient list, why?



Lactic acid is used in certain products to optimize the throat hit as well as your overall experience.

What is the difference between the NJOY King and the NJOY Daily?



There are several differences between the King and Daily, besides its size. NJOY Daily has been innovated to deliver quick & strong satisfaction more like a cigarette, it features a new longer lasting battery with QuickVapor technology delivering significantly longer battery life (approx. 300 puffs), has new upgraded flavors, more vapor volume and a discreet but stylish new design.

EXHIBIT E

PAX Labs, Inc.

660 Alabama Street, Second Floor
San Francisco, CA 94110

E-Liquid Analysis **Electronic Cigarette (eC) Liquid Testing**

Analysis Report
(1115-553)

GC/FID Analysis (ENT184)

Nicotine, Propylene glycol, Vegetable glycerin, Water

HPLC/UV Analysis (ENT301-Mod)

Lactic Acid



Enthalpy Analytical, Inc.

Phone: (919) 850 - 4392 / Fax: (919) 850 - 9012 / www.enthalpy.com
800-1 Capitola Drive Durham, NC 27713-4385

I certify that to the best of my knowledge all analytical data presented in this report summary:

- Have been checked for completeness
- Are accurate, error-free, and legible
- Have been conducted in accordance with approved protocol

This analytical report was prepared in Portable Document Format (.PDF) and contains 10 pages.

Jennifer B. Feller

QA Review Performed by: Jennifer B. Feller

Report Issued: 1/6/2016



Summary of Results





Report for: PAX Labs, Inc.
Client Project: Electronic Cigarette (eC) Liquid Testing
Sample Type: e-Liquid

Project Code: 1115-553
Project Start Date: 11/13/15
Analysis Method: ENT184

Enthalpy Code	Client Code	Nicotine (mg/mL)	Propylene glycol (mg/mL)	Glycerin (mg/mL)	Water # (mg/mL)
1115-553-01-01	PO-J1-1511112A1	46.8	491	487	57.6
1115-553-01-02		47.3	497	489	59.9

#: Water results are blank corrected.

Report for: PAX Labs, Inc.
 Client Project: Electronic Cigarette (eC) Liquid Testing
 Sample Type: e-Liquid

Project Code: 1115-553
 Project Start Date: 11/13/15
 Analysis Method: ENT301-Mod

Enthalpy Code	Client Code	Notes	Lactic Acid (ug/mL)
1115-553-01 (DF 1010) 1	PO-J1-1511112A1	--	22,597
1115-553-01 (DF 1010) 2			22,389
		Average	22,493
		%DIFF	0.9

Narrative Summary



Enthalpy Analytical Narrative Summary

Company	PAX Labs, Inc.
Analysts	KEH, BJB/ABP
Parameters	ENT184, ENT301-Mod

Client Proj	Electronic Cigarette (eC) Liquid Testing
Job #	1115-553
# Samples	1 eC Liquid Sample

Custody	<p>A scintillation vial labeled "<i>E-Liquid test nicotine, Lactic acid PG. Glycerin PO-J1-151112A1</i>" was used for this project. It was prepared and analyzed in duplicate.</p> <p>Prior to, during, and after analysis, the sample was kept under lock with access only to authorized personnel by Enthalpy Analytical, Inc.</p>
ENT184 (Primary Constituents)	<p>The e-Liquid sample was prepared and analyzed in duplicate for nicotine, propylene glycol (PG), and vegetable glycerin (aka VG, glycerin, or glycerol), and water following the analytical procedures in Enthalpy SOP ENT184.</p> <p>The samples were analyzed on the Hewlett Packard Model 6890 Gas Chromatograph "BMO" equipped with a Flame Ionization Detector (FID) and an appropriate column.</p>
ENT301-Mod (Lactic Acid)	<p>The e-Liquid sample was prepared and analyzed in duplicate for lactic acid following the general analytical procedures in Enthalpy SOP ENT301.</p> <p>The samples were analyzed using the Agilent Model 1100, High Performance Liquid Chromatograph "Selma," equipped with an Ultraviolet (UV) Detector operating at 360 nm and an appropriate column.</p>
QC Notes	<p>All QC samples were within acceptance criteria unless otherwise noted.</p> <p>As the lactic acid analysis was not a standard laboratory method, a second source standard was not available to verify the calibration for lactic acid. A continuing calibration sample was analyzed after the samples, and had a recovery of 98.7% of the expected concentration.</p>
Reporting Notes	<p>Sample and calibration curve chromatograms are available upon request.</p> <p>The results presented in this report are representative of the samples as provided to the laboratory.</p>



General Reporting Notes

The following are general reporting notes that are applicable to all Enthalpy Analytical, Inc. data reports, unless specifically noted otherwise.

- Any analysis which refers to the method as “**Type**” represents a planned deviation from the reference method. For instance a Hydrogen Sulfide assay from a Tedlar bag would be labeled as “EPA Method 16-Type” because Tedlar bags are not mentioned as one of the collection options in EPA Method 16.
- The acronym **MDL** represents the Minimum Detection Limit. Below this value the laboratory cannot determine the presence of the analyte of interest reliably.
- The acronym **LOQ** represents the Limit of Quantification. Below this value the laboratory cannot quantitate the analyte of interest within the criteria of the method.
- The acronym **ND** following a value indicates a non-detect or analytical result below the MDL.
- The letter **J** in the Qualifier or Flag column in the results indicates that the value is between the MDL and the LOQ. The laboratory can positively identify the analyte of interest as present, but the value should be considered an estimate.
- The letter **E** in the Qualifier or Flag column indicates an analytical result exceeding 100% of the highest calibration point. The associated value should be considered as an estimate.
- The acronym **DF** represents Dilution Factor. This number represents dilution of the sample during the preparation and/or analysis process. The analytical result taken from a laboratory instrument is multiplied by the DF to determine the final undiluted sample results.
- The addition of **MS** to the Sample ID represents a Matrix Spike. An aliquot of an actual sample is spiked with a known amount of analyte so that a percent recovery value can be determined. The MS analysis indicates what effect the sample matrix may have on the target analyte, i.e. whether or not anything in the sample matrix interferes with the analysis of the analyte(s).
- The addition of **MSD** to the Sample ID represents a Matrix Spike Duplicate. Prepared in the same manner as an MS, the use of duplicate matrix spikes allows further confirmation of laboratory quality by showing the consistency of results gained by performing the same steps multiple times.
- The addition of **LD** to the Sample ID represents a Laboratory Duplicate. The analyst prepares an additional aliquot of sample for testing and the results of the duplicate analysis are compared to the initial result. The result should have a difference value of within 10% of the initial result (if the results of the original analysis are greater than the LOQ).
- The addition of **AD** to the Sample ID represents an Alternate Dilution. The analyst prepares an additional aliquot at a different dilution factor (usually double the initial factor). This analysis helps confirm that no additional compound is present and coeluting or sharing absorbance with the analyte of interest, as they would have a different response/absorbance than the analyte of interest.
- The Sample ID **LCS** represents a Laboratory Control Sample. Clean matrix, similar to the client sample matrix, prepared and analyzed by the laboratory using the same reagents, spiking standards and procedures used for the client samples. The LCS is used to assess the control of the laboratory’s analytical system. Whenever spikes are prepared for our client projects, two spikes are retained as LCSs. The LCSs are labeled with the associated project number and kept in-house at the appropriate temperature conditions. When the project samples are received for analysis, the LCSs are analyzed to confirm that the analyte could be recovered from the media, separate from the samples which were used on the project and which may have been affected by source matrix, sample collection and/or sample transport.



General Reporting Notes

(continued)

- **Significant Figures:** Where the reported value is much greater than unity (1.00) in the units expressed, the number is rounded to a whole number of units, rather than to 3 significant figures. For example, a value of 10,456.45 ug catch is rounded to 10,456 ug. There are five significant digits displayed, but no confidence should be placed on more than two significant digits.
- **Manual Integration:** The data systems used for processing will flag manually integrated peaks with an "M". There are several reasons a peak may be manually integrated. These reasons will be identified by the following two letter designations. The peak was *not integrated* by the software "NI", the peak was *integrated incorrectly* by the software "II" or the *wrong peak* was integrated by the software "WP". These codes will accompany the analyst's manual integration stamp placed next to the compound name on the chromatogram.



**This Is The Last Page
Of This Report.**



EXHIBIT F

MEET NJOY DAILY

Over 90 percent as satisfying as a cigarette*



Strong throat hit for authentic feel

Flavors formulated & blended in a pharmaceutical-grade facility in the USA

Flavor concentration increased for maximum satisfaction



FEEL THE DIFFERENCE



Soft touch wrapper for premium hand feel

Soft-tip filter for enhanced mouth feel

Small & light enough to hold in your mouth or in two fingers



INNOVATIVE DESIGN

New QuickVapor technology battery delivers vapor faster and extends battery life to approximately 300 puffs (~ 1 pack of cigarettes)



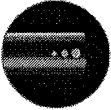
50/50 PG/VG balance to maximize vapor thickness and volume

STYLE & SUBSTANCE

Tip illuminates to let you know it's on without being conspicuous



Tone-on-tone logo adds discreet sophistication



Food-grade coloring on the mouth tip for style & safety

Color dots are a subtle flavor reminder

*During the first seven minutes. Clinical trial conducted by independent lab measuring nicotine absorption in blood stream represented by mean of test subjects assessed on day 8 of use following 12 hours of abstinence; measured using participating subject's preferred brand of cigarette.



IT'S THAT SATISFYING

Our latest innovation is now delivering the most authentic "smoking" experience to date. We're proud (and really freakin' excited) to introduce the Daily – a labor of love that blends Satisfaction, Performance, Authenticity, Flavor and Design for an experience that's more than 90% as satisfying as a cigarette during the first 7 minutes of use.

*June 2015 in-home consumer study consisting of adult smokers using tobacco and menthol flavor of both brands.

(Screen capture from <https://www.njoy.com/daily>, last visited June 13, 2016)

EXHIBIT G

INTRODUCING

NJOY® DAILY

THE DIFFERENTIATED DISPOSABLE

DESIGNED WITH RETAILERS IN MIND

REINTEGRATING CONSUMER TRIAL

- Everyday value - approximately 300 puffs for \$5.99 per stick
- Quick & strong satisfaction more like a cigarette
- Disposable lightweight stick

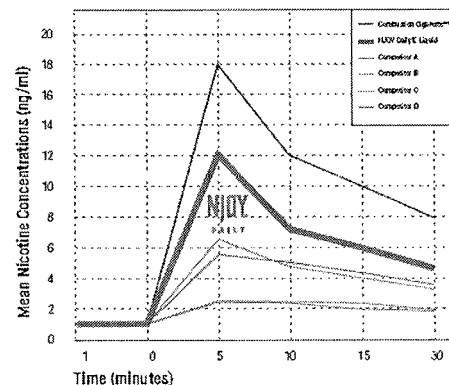
MAXIMIZE PURCHASE FREQUENCY & PROFITS

- ~40% margins*
- 1 count configuration to help restore purchase frequency
- Compact 5 count cartons for limited investment and optimal turns
- Flavor freshness seal for extended shelf life
- ~70% higher gross profit per week vs. leading rechargeable refills**

SELL THROUGH RATE SUPPORT

- Robust introductory pricing promotions
- Modular merchandising displays and impactful signage
- Multi-million dollar consumer advertising campaign
- Trial generating activations
- Targeted coupon delivery to adult smokers

NICOTINE DELIVERY
CIGARETTE VS TOP C STORE BRANDS



Source:

*Margin assumes NJOY retail and NJOY MSRP price

** Assumes "Conversion rate" from completely switching from pack-a-day of cigarettes to 5 Vapor Products. Assumes 7 units per week of consumption. 1 Count Disposable Disposable = 1 stick.

Package: 1 count disposable, 1 stick, 1 count disposable, 1 stick, 1 count disposable, 1 stick, 1 count disposable, 1 stick.

*** All data based on participating subjects' self-reported use of NJOY.

Chart Notes: Clinical trial conducted by independent lab testing every nicotine absorption in blood at 5, 10, 15, 20, 25, and 30 minutes following 12 hours of abstinence. NJOY 18-20 per product. Subjects smokers aged 18-35 not currently attempting to quit. Products puffed (starting at time zero) every 30 seconds for 5 minutes.

WARNING: NJOY® products are not smoking cessation products and have not been tested as such, and have the long-term effects of using the product have not been established. NJOY® products are intended for use by adults of legal smoking age (18 years in California, and not by children who are under 18 years of age, pregnant women, or persons with or at risk of heart disease, high blood pressure, diabetes or taking medicine for depression or asthma. NJOY® products contain nicotine, which is addictive, and the State of California has found it addictive to the extent that it is a significant health hazard. Nicotine is addictive and habit forming, and it may be harmful to health. In contact with the skin, it may be absorbed. Ingestion of the non-vaporized components of NJOY® products is also possible. If any liquid is swallowed, seek medical assistance immediately.



EXHIBIT H

Consumer Testimonials

Sampling of customer testimonials from www.njoy.com/ (last visited 6/10/2016)



Julia Verified Reviewer

04/29/16



Love your Daily ecigarette, Blue + black berry

This product is awesome! Really great flavor, really awesome vapor. I would definitely recommend this ecig to a friend who is looking to switch. Best ecig out there by far in terms of nicotine satisfaction!



Sammy G. Verified Reviewer

02/04/16



The njoy Daily is the best e-cigarette yet!

I've tried them all...well most of them. This is the first e-cigarette that really offers an effective substitute to a real cigarette. Terrific!



Sam J. Verified Reviewer

03/07/16



Best E-cigs in the Game!

NJOY is my go-to e-cig.. I was a long time user of the Kings e-cigarette and I've just recently made the switch to their new Daily electronic cigarette.. The Daily e-cig has the nicotine fix I need and it really does feel like a regular cigarette.. The Blue + Black Berry is my favorite flavor !!

 Share |

Was This Review Helpful?  4  0

Customer testimonials from <http://www.vaporauthority.com/products/genuine-njoy-daily-disposable-e-cig> (last visited June 10, 2016):

★★★★★ (5/5)

Steven P from **Philly** on **May 17, 2016**

Great disposable here, probably the best one I've ever tried. Got one a while ago just for shits but now I pick a couple of em up every time I place an order here. These are so easy for out and about or stealthy vaping. Damn close to an analog too!

[Report this review](#)

★★★★★ (5/5)

Morgan from **Denver** on **Apr 29, 2016**

Unbelievable! It's like I'm smoking a cigarette again, but I'm not... I have been vaping instead of smoking for like a year now and this is a great way to revisit that without feeling like shit afterwards! Whooo Hoooo!

[Report this review](#)

★★★★★ (5/5)

Alana B from **Austin Tx** on **Apr 11, 2016**

Oh Wow! I've tried other ecigs like this from the gas station and they were disappointing, but I'd never seen these Daily before. Now this is the closest thing to a real cigarette that I've ever had! I mean, if its this good I don't know why anyone would smoke real cigs.. Completely satisfying!! I actually have a nice vape set up and I just ordered these out of curiosity and I wanted an emergency go-to if my vape broke or got lost or something. Really good on the out and about. I'm definitely going to keep a stock of these around for rough times. Would be great for someone just trying to quit cigarettes, but it could get costly if you just relied on these. Get these and also a good mod and tank - and your golden! Much appreciated Vapor Authority!

[Report this review](#)

Exemplary Customer review from Reddit:

https://www.reddit.com/r/electronic_cigarette/comments/3s2kcd/njoy_daily_disposable_review/ (last visited June 10, 2016):

https://www.reddit.com/r/electronic_cigarette/comments/3s2kcd/njoy_daily_disposable_review/



NJOY Daily disposable review REVIEW self:electronic_cigarette
Submitted 7 months ago by [Greybush_The_Rotund](#)

I have a habit of posting a review here every time I get my hands on something new, 'cause I hate it when I can't find reviews for this or that, and I'm sure others feel the same way.

I'm reviewing a new disposable cigalike, the NJOY Daily, after a week of hands-on time with it.

TL;DR:

Surprisingly not bad, but not perfect either. Seems good for flipping smokers who aren't ready for non-cigalike devices.

Preface

My vaping history: Quit smoking in 2011 with the help of no-name 7-11 cigalikes, quit vaping after 3 months because aforementioned cigalikes were an expensive pain in the ass and I didn't know fancier vapes were a thing, then a few years later cravings kicked my ass during a particularly stressful period at work, and I started vaping again thanks to this subreddit cluing me in to the existence of better setups.

I've gone through the whole typical beginner equipment cycle (cigalikes, eGo type setups, iStick 20 with Mini Nautilus/Subtank Nano, and now I use an eGo One with CLR coils that I rebuild myself) over the course of the past year-plus-change.

The NJoy Daily

I got my hands on a couple Dailies, having bought one out of skeptical curiosity for my wife, and the other one was thrown in for free. I also bought a few extra afterwards for the sake of review accuracy (don't you hate it when people review something after the first few uses and never get to the "and then it shit the bed and exploded the next day" issues?)

Anyway, NJOY has been marketing the Daily rather aggressively since before its retail debut in September 2015, and I had this urge to put their claims to the test. These claims are:

- Look and feel: Feels more like a real cigarette, without looking like one.
- Vaping experience: Hits more like a real cigarette.
- Longevity: Lasts for 300 puffs and is equivalent to a pack of cigarettes.

Look and Feel

The Daily doesn't even try to pretend to look like a cigarette. It's dark blue, with a squishy feeling mouth end, and the tip lights up white. It feels very light, much lighter than the heavy cigalikes I started with in 2011. You can actually hold it in your teeth and not feel like you're gnawing on a metal clicker pen. It doesn't look completely cheap/chintzy, looks a bit classier than a Blu disposable, and won't be mistaken for the real thing.

I'm ambivalent on the look/feel--there are times when I'd want a small device that's obviously *not* a cigarette, but there are also times when it's better to blend in.

Vaping Experience

The first drag I took felt almost exactly like taking a drag off an actual cigarette, which took me by surprise. *To test this further, I handed it to my wife, who still smokes. She was very pleasantly surprised and then promptly claimed it as her own.*

Throat hit and feel were practically spot-on. It feels noticeably "drier" and warmer than my usual vape, and the vapor clouds are about on par with an analog. The Rich Tobacco feels a bit more like an actual cigarette than the Menthol does.

Flavor is somewhat underwhelming. The Rich Tobacco is a bit sweet and more like a pipe tobacco, but is noticeably muted. The Menthol has a strange sort of berry-ish note that I wasn't expecting, but you can feel the menthol.

These things pack 45 mg/mL of nicotine, and you feel it almost immediately. You also feel "done" rather quickly--normally, with my eGo One, I can puff away on it for 20 minutes without getting nic'd out, but

with the Daily, I'm done within 5-10 minutes.

Hilariously, I also frequently caught myself absentmindedly flicking/tapping it like the real thing.

Short form, it feels and hits like a real cigarette, but falls short in the flavor department.

Longevity

Normally, whenever a cigalike claims that it's equivalent to a whole pack of cigarettes, I usually bust out laughing because I've never gotten anywhere near that kind of performance out of cigalikes in the past.

The "300 puffs" type of marketing statement is also probably based on the work of an unpaid intern with a small squeeze bulb and a click counter. Hardly anyone I know smokes or vapes like a small squeeze bulb, so puff count is a metric that I usually dismiss as irrelevant.

The more practical metric I'd use instead, when judging whether or not a cigalike is equivalent to a pack of cigarettes, starts with how long that pack would last me if I were still smoking. When I quit, I was smoking about a pack per day. So, in order to meet that threshold for me, a Daily would need to last an entire day from morning to bedtime, assuming I maintained a typical schedule of stepping outside roughly every other hour or so for 5-10 minutes.

For the sake of science, I've gone through 6 of them over the past week, and am still working on number seven. So far, they all have consistently lasted about 24 hours before giving up the ghost, give or take an hour or two.

Mind you, I'm not chain vaping the things, just using them in the same manner that I used to smoke—stepping outside every hour or hour and a half for 5 to 10 minutes during the 16-ish hours that I'm awake. The drags I took were about 2-4 seconds long, with about the same amount of suction that I used as a smoker, and I took one to three drags per minute.

If I tried to chain-vape a Daily, I doubt they'd last more than 3 hours (and I'd either have the mother of all nic buzzes or be puking my guts out).

They deliver. I'm impressed. They're a step up from the other disposables I've tried.

Price

MSRP for a Daily is \$5.99. For me, given my week-long pack-a-day simulation for this review, that puts the Daily on par with buying a pack a day. So, it's not cheap, but if you smoke a pack or less a day, it's competitive with buying cigarettes, yet still more expensive over the medium to long term than going straight to something like a basic eGo setup with decent clearomizers.

From a practical standpoint, the cigalikes I've tried before had a much worse bang-for-the-buck factor, costing anywhere from 1.5x to over twice what you'd spend on cigarettes and failing to come anywhere close to the stated longevity.

The Daily seems to be an okay middle ground as far as disposables go—not too expensive relative to a pack of cigarettes, and noticeably more reliable and consistent than the junky stuff.

Verdict

Smokers trying to quit through vaping tend to run into a number of pain points in the critical earliest days. At this point, they're usually trying to replace smoking with something that feels *like* smoking, and they're transitioning through not just a nicotine addiction, but also the physical/psychological aspect of the habit.

So, what they generally want is something that gives them the same feeling as smoking *without* being a gigantic pain in the ass or requiring a level of acclimatization that exceeds their threshold of frustration.

I think this is a good device for flipping smokers, especially those who choke on larger setups. My wife, for example, has tried several different devices and they all seem to make her cough or simply don't satisfy when dialed down. This device, she actually likes.

Supplemental Application Data Sheet

Application Information

Application number:: 14/925,968
Filing Date:: October 28, 2015
Title:: NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
AND METHODS THEREOF
Attorney Docket Number:: 13211-713.303

- Please update the Applicant Information as follows:

Applicant Information

Assignee?:: YES
Organization name:: PAX Labs, Inc.
Street of mailing address:: 660 Alabama Street, Second Floor
City of mailing address:: San Francisco
State or Province of mailing address:: CA
Postal or Zip Code of
mailing address:: 94110
Country of mailing address:: US

- Please update the Assignee Information as follows:

Assignee Information

Assignee name:: PAX Labs, Inc.
Street of mailing address:: 660 Alabama Street, Second Floor
City of mailing address:: San Francisco
State or Province of mailing address:: CA
Postal or Zip Code of

mailing address:: 94110

Country of mailing address:: US

Signature:

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.

Signature		Date	June 15, 2016
Name	Richard D. Shoop	Registration No.	45,763

POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date
14/925,968	October 28, 2015

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☒ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above:

66854

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☒ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

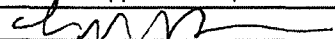
I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

PAX LABS, INC.

- ☐ Inventor or Joint Inventor (title not required below)
- ☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)
- ☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)
- ☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	3-30-2016
Name	Adam Bowen		
Title	Chief Technology Officer and Co-Founder		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☒ Total of one forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

STATEMENT UNDER 37 CFR 3.73(c)Applicant/Patent Owner: PAX LABS, INC.Application No./Patent No.: 14/925,968Filed/Issue Date: October 28, 2015Titled: NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOFPAX LABS, INC., a Corporation

(Name of Assignee)

(Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose one of options 1, 2, 3 or 4 below):

1. ☒ The assignee of the entire right, title, and interest.
2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):
- ☐ The extent (by percentage) of its ownership interest is ____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.
- ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (e.g., bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose one of options A or B below):

- A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.
- B. ☒ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Adam BOWEN and Chenyue XING To: PLOOM, INC.The document was recorded in the United States Patent and Trademark Office at
Reel 037990, Frame 0969, or for which a copy thereof is attached.2. From: PLOOM, INC. To: PAX LABS, INC.The document was recorded in the United States Patent and Trademark Office at
Reel 037991, Frame 0005, or for which a copy thereof is attached.

[Page 1 of 2]

This collection of information is required by 37 CFR 3.73(b). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached.

5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached.

6. From: _____ To: _____

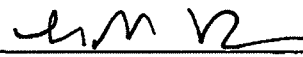
The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☒ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.



 Signature

Adam Bowen

Printed or Typed Name

3-30-2016

 Date

CTO and Co-Founder

 Title or Registration Number

Electronic Acknowledgement Receipt

EFS ID:	26076217
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Mary Buggie
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	15-JUN-2016
Filing Date:	28-OCT-2015
Time Stamp:	16:29:05
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_AFCP_Respons eFOA_Decl_1-132_6-15-2016. pdf	3578368	yes	50
			028c580780e1fb3369afdfb01d85e7cb65eb430c		

	Multipart Description/PDF files in .zip description		
	Document Description	Start	End
	After Final Consideration Program Request	1	1
	Response After Final Action	2	2
	Claims	3	6
	Applicant Arguments/Remarks Made in an Amendment	7	19
	Affidavit-traversing rejectns or objectns rule 132	20	45
	Application Data Sheet	46	47
	Power of Attorney	48	48
	Assignee showing of ownership per 37 CFR 3.73	49	50
Warnings:			
Information:			
Total Files Size (in bytes):		3578368	
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>			

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 14/925,968	Filing Date 10/28/2015	☐ To be Mailed
---	---	----------------------------------	---------------------------------------

ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (j), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X \$ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X \$ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)
	06/15/2016	CLAIMS REMAINING AFTER AMENDMENT					
	Total (37 CFR 1.16(i))	* 17	Minus	** 20	= 0	X \$80 =	0
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$420 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT	(Column 1)	(Column 2)	(Column 3)	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)
		CLAIMS REMAINING AFTER AMENDMENT					
	Total (37 CFR 1.16(i))	*	Minus	**	=	X \$ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X \$ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
 ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
 *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
 The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/PHYLLIS CANTY/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
14/925,968	10/28/2015	Adam BOWEN	13211-713.303

CONFIRMATION NO. 2707

POA ACCEPTANCE LETTER



66854
SHAY GLENN LLP
2755 CAMPUS DRIVE
SUITE 210
SAN MATEO, CA 94403

Date Mailed: 06/24/2016

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 06/15/2016.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at (571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/byemane/



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
14/925,968	10/28/2015	1747	1600	13211-713.303	20	3

66854
SHAY GLENN LLP
2755 CAMPUS DRIVE
SUITE 210
SAN MATEO, CA 94403

CONFIRMATION NO. 2707
CORRECTED FILING RECEIPT



Date Mailed: 06/24/2016

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Adam BOWEN, San Francisco, CA;
Chenyue XING, San Francisco, CA;

Applicant(s)

PAX Labs, Inc., San Francisco, CA;

Assignment For Published Patent Application

PAX Labs, Inc., San Francisco, CA

Power of Attorney: The patent practitioners associated with Customer Number 66854

Domestic Priority data as claimed by applicant

This application is a CON of 14/512,311 10/10/2014 PAT 9215895
which is a CON of 14/271,071 05/06/2014
which claims benefit of 61/820,128 05/06/2013
and claims benefit of 61/912,507 12/05/2013

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: No

Permission to Access Search Results: No

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 11/09/2015

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 14/925,968**

Projected Publication Date: Not Applicable

Non-Publication Request: No

Early Publication Request: No
Title

NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF

Preliminary Class

131

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop

technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 1

of 2

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	595	US- 9,220,302	12/29/2015	DePiano et al.	
	596	US- 9,226,526	1/5/2016	Liu	
	597	US- 9,271,525	3/1/2016	Liu	
	598	US- 9,271,529	3/1/2016	Alima	
	599	US- 9,272,103	3/1/2016	Storz	
	600	US- 9,277,769	3/8/2016	Liu	
	601	US- 9,282,772	3/15/2016	Tucker et al.	
	602	US- 9,282,773	3/15/2016	Greim et al.	
	603	US- 9,289,014	3/22/2016	Tucker et al.	
	604	US- 9,308,336	4/12/2016	Newton	
	605	US- 9,326,547	5/3/2016	Tucker et al.	
	606	US- 9,351,522	5/31/2016	Safari	
	590	US- 2013/0199528	8/8/2013	Goodman et al.	
	591	US- 2014/0144429	5/29/2014	Wensley et al.	
	592	US- 2015/0272220	10/1/2015	Spinka et al.	
	608	US- 2015/0282525	10/8/2015	Plojoux et al.	
	609	US- 2015/0313275	11/5/2015	Anderson et al.	
	611	US- 2015/0351456	12/10/2015	Johnson et al.	
	614	US- 2016/0021931	1/28/2016	Hawes et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	639	WO2015/149647A1(w/ Eng Abs)	10/8/2015	Kimree Hi-Tech Inc.		
	640	WO2015/168828A1(w/ Eng Abs)	11/12/2015	Kimree Hi-Tech Inc.		

Examiner
SignatureDate
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet 2 of 2**Complete if Known**

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

U. S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	607	US- 2016/0058071	3/3/2016	Hearn	
	618	US- 2016/0058072	3/3/2016	Liu	
	621	US- 2016/0081395	3/24/2016	Thorens et al.	
	623	US- 2016/0106154	4/21/2016	Lord	
	624	US- 2016/0106155	4/21/2016	Reevell	
	627	US- 2016/0120218	5/5/2016	Schennum et al.	
	630	US- 2016/0135503	5/19/2016	Liu	
	632	US- 2016/0143359	5/26/2016	Xiang	
	635	US- 2016/0143365	5/26/2016	Liu	
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND** TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

(12) 按照专利合作条约所公布的国际申请

(19) 世界知识产权组织
国际局

(43) 国际公布日
2015 年 10 月 8 日 (08.10.2015)



(10) 国际公布号
WO 2015/149647 A1

(51) 国际专利分类号:
A24F 47/00 (2006.01)

(21) 国际申请号: PCT/CN2015/075101

(22) 国际申请日: 2015 年 3 月 26 日 (26.03.2015)

(25) 申请语言: 中文

(26) 公布语言: 中文

(30) 优先权:
201410133757.8 2014 年 4 月 3 日 (03.04.2014) CN

(71) 申请人 (对除美国外的所有指定国): 吉瑞高科技
股份有限公司 (KIMREE HI-TECH INC.); 英属维
尔京群岛托尔托拉岛罗德城奎兹天空大厦邮箱 905
号, Tortola (VG)。

(72) 发明人: 及

(71) 申请人 (仅对美国): 刘秋明 (LIU, Qiuming)
[CN/CN]; 中国广东省惠州市仲恺高新区和畅西三
路 16 号 A 栋三、四、五层, Guangdong 516000
(CN)。

(74) 代理人: 北京集佳知识产权代理有限公司
(UNITALEN ATTORNEYS AT LAW); 中国北京市朝

阳区建国门外大街 22 号赛特广场 7 层, Beijing
100004 (CN)。

(81) 指定国 (除另有指明, 要求每一种可提供的国家保
护): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG,
BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR,
CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB,
GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS,
JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU,
LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ,
NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA,
RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST,
SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, ZA, ZM, ZW。

(84) 指定国 (除另有指明, 要求每一种可提供的地区保
护): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA,
RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), 欧亚 (AM, AZ,
BY, KG, KZ, RU, TJ, TM), 欧洲 (AL, AT, BE, BG, CH,
CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE,
IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO,
RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)。

本国际公布:

— 包括国际检索报告 (条约第 21 条(3))。

(54) Title: ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREOF

(54) 发明名称: 电子烟和电子雾化控制方法

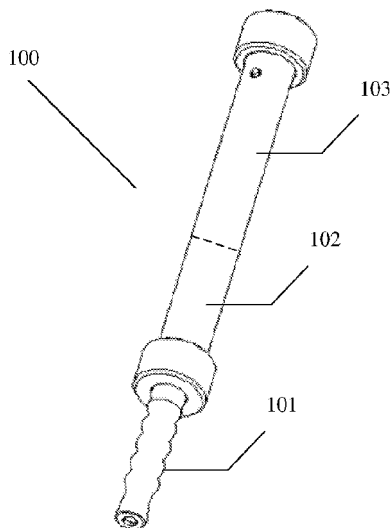


图 1 / FIG. 4

(57) Abstract: An electronic cigarette (100) and atomization control method thereof; the electronic cigarette (100) comprises a smoking end (101), a voice recognition module (301) generating different selection signals according to a received voice, an atomization module (102), a microcontroller (302) connected to the voice recognition module (301), an air flow sensor (303), and a battery module (103); the different selection signals comprise a first selection signal or a second selection signal; the atomization module (102) comprises a first atomization assembly (201) and a second atomization assembly (203), and a first oil storage space (202) and a second oil storage space (204) filled with different types of tobacco liquid; the microcontroller (302) is used to communicate with the first atomization assembly (201) according to the first selection signal, or to communicate with the second atomization assembly (203) according to the second selection signal; the air flow sensor (303) is used to generate a first pulse signal, and is connected to the microcontroller (302); and the microcontroller (302) is also used to generate a first control signal according to the first pulse signal, and the atomization assemblies (201, 203) communicating with the microcontroller (302) are used to atomize the tobacco liquid in the corresponding oil storage spaces (202, 204) according to the first control signal. The electronic cigarette (100) enables a user to select by voice different tastes of tobacco liquid in one electronic cigarette (100).

(57) 摘要:

[见续页]

WO 2015/149647 A1



一种电子烟(100)和电子烟(100)雾化控制方法,该电子烟(100)包括:吸烟端(101)、用于根据接收到的语音产生不同选择信号的语音识别模块(301)和雾化模块(102),不同选择信号包括第一或第二选择信号,雾化模块(102)包括第一和第二雾化组件(201,203),分别装载不同烟液的第一和第二储油空间(202,204);与语音识别模块(301)连接的微控制器(302),用于根据第一选择信号与第一雾化组件(201)连通,或根据第二选择信号与第二雾化组件(203)连通;还包括用于产生第一脉冲信号的、与微控制器(302)连接的气流感应器(303),和电池模块(103);微控制器(302)还用于根据第一脉冲信号生成第一控制信号,与微控制器(302)连通的雾化组件(201,203)用于根据第一控制信号雾化相应的储油空间(202,204)内的烟液。该电子烟(100)能够让用户采用语音在一个电子烟(100)内选择不同口味的烟液。

-1-

电子烟和电子烟雾化控制方法

本申请要求于 2014 年 4 月 3 日提交中国专利局、申请号为 201410133757.8、发明名称为“电子烟和电子烟雾化控制方法”的中国专利申请

的优先权，其全部内容通过引用结合在本申请中。

5 技术领域

本发明涉及电子烟技术领域，尤其涉及一种电子烟和电子烟雾化控制方法。

背景技术

10 电子烟是一种新型的电子产品，其与普通的香烟有着相同的外观，以及与香烟相同的味道，但是电子烟相对于传统的香烟更为的健康以及环保。

电子烟是通过高科技硅芯片和感应器控制烟雾输出量以及工作状态，烟雾被雾化，将含有烟碱和香精的溶液雾化成颗粒。电子烟中不含普通香烟中的焦油和其他有害成分，也不会产生二手烟。

15 现有的电子烟中，但现有的电子烟中，用户只能吸食到一种口味的烟液，若想吸食到其他口味的烟液，需携带多支不同口味的电子烟。

发明内容

本发明提供了一种电子烟和电子烟雾化控制方法，能够让用户采用语音在一个电子烟内选择不同口味的烟液。

本发明公开了一种电子烟，包括：

20 电子烟本体；

所述电子烟本体设置有吸烟端、用于根据接收到的语音产生不同选择信号的语音识别模块和雾化模块，所述不同选择信号包括第一选择信号或者第二选择信号，所述雾化模块至少包括第一雾化组件和第二雾化组件，所述第一雾化组件内和所述第二雾化组件内分别设置有装载不同烟液的第一储油空间和第
25 二储油空间；

与所述语音识别模块相连接的微控制器，用于根据所述第一选择信号与所述第一雾化组件连通，或根据所述第二选择信号与所述第二雾化组件连通；

所述电子烟本体还设置有用产生第一脉冲信号的、与所述微控制器相连接的气流感应器，和用于给所述微控制器、所述第一雾化组件以及第二雾化组

-2-

件供电的电池模块;

所述微控制器还用于根据所述第一脉冲信号生成第一控制信号,与所述微控制器连通的雾化组件用于根据所述第一控制信号雾化相应的储油空间内的烟液。

5 本发明所述的电子烟中,其中,

所述语音识别模块还用于根据接收到的语音产生第三选择信号;

所述微控制器还用于根据所述第三选择信号同时与所述第一雾化组件和所述第二雾化组件连通。

本发明所述的电子烟中,其中,

10 所述第一雾化组件还包括用于雾化所述第一储油空间内的烟液的第一电热丝组件;

所述第一雾化组件还包括用于雾化所述第二储油空间内的烟液的第二电热丝组件;

15 所述第一储油空间的两端分别和所述第二储油空间的两端相邻,以使所述第一储油空间和第二储油空间平行并排设置在所述电子烟本体内。

本发明所述的电子烟中,其中,

所述第一雾化组件还包括:

20 第一雾化器支架,所述第一雾化器支架靠近所述电池模块的一端设置第一螺纹段,所述电池模块靠近所述第一雾化器支架的一端设有第一匹配螺纹,所述第一雾化器和所述电池模块通过所述第一螺纹段和所述第一匹配螺纹的配合来可拆卸连接;

所述第一储油空间设于所述第一雾化器支架上;

所述第二雾化组件还包括:

25 第二雾化器支架,所述第二雾化器支架靠近所述电池模块的一端设置第二螺纹段,所述电池模块靠近所述第二雾化器支架的一端还设有第二匹配螺纹,所述第二雾化器和所述电池模块通过所述第二螺纹段和所述第二匹配螺纹的配合来可拆卸连接;

所述第二储油空间设于所述第二雾化器支架上。

本发明所述的电子烟中,其中,

-3-

所述语音识别模块包括语音接收器和语音识别单元;

所述语音接收器用于接收语音信号,并将接收到的语音信号转换为电信号;

5 所述语音识别单元用于根据所述电信号生成相应的所述第一选择信号或者所述选择第二信号,并将所述选择第一信号或者第二选择信号发送至所述微控制器。

本发明所述的电子烟中,其中,所述电池模块还包括:

用于接收用户操作指令的按键;

与所述按键连接设置有用用于根据所述操作指令生成启动信号的微触开关;

10 且所述微触开关与所述语音接收器连接,以使所述语音接收器根据所述启动信号接受语音信号。

本发明所述的电子烟中,其中,

所述电子烟本体内还设置有低压保护模块;

15 所述电子烟本体外表面还设有与所述低压保护模块连接设置的第一提醒装置;

所述低压保护模块用于控制所述第一提醒装置的工作状态。

本发明所述的电子烟中,其中,

所述电子烟本体内还设置有过流保护模块;

20 所述电子烟本体外表面还设有与所述过流保护模块连接设置的第二提醒装置;

所述过流保护模块用于控制所述第二提醒装置的工作状态。

本发明还公开了一种电子烟雾化控制方法,包括:

所述电子烟内设有至少两个雾化组件,其中不同的雾化组件分别设置有不同的储油空间,其中不同储油空间上装载有不同的烟液;

25 所述电子烟获取语音信号;

所述电子烟根据所述语音信号生成不同的选择信号,其中所述不同的选择信号对应着所述不同的雾化组件;

所述电子烟根据所生成的选择信号选定对应的雾化组件;

所述电子烟当检测到内部压力变化时,控制所述选定的雾化组件工作。

-4-

本发明所述的电子烟雾化控制方法，其中，

所述电子烟包括第一雾化组件和第二雾化组件；

所述电子烟根据所生成的选择信号选定对应的雾化组件具体包括：

若所述选择信号为第一选择信号，则选定第一雾化组件；

5 若所述电信号为第二选择电信号，则选定第二雾化组件；

若所述电信号为第三选择电信号，则同时选定第一雾化组件和第二雾化组件。

从以上技术方案可以看出，本发明实施例具有以下优点：

10 本发明所提供的电子烟中设有至少两种雾化组件，其中不同的雾化组件中设有装载着不同烟液的储油空间，且该电子烟上还设有相互连接的语音识别模块和微控制器，其中该语音识别模块根据接收到不同的语音来发出不同的选择信号，而该微控制器根据该不同的选择信号来选择相对应的雾化组件工作，这样，用户能够在一支电子烟上吸食到不同口味的烟液，避免了用户需携带多支电子烟而造成的不便或通过使用复杂的机械结构而造成组装不便等问题；另

15 外，用户可以采用语音在一个电子烟内选择不同口味的烟液，选择方式方便快捷，极大地降低了因更换烟液造成的烟液泄露到电子烟表面而弄脏用户或吸食到泄露的烟液的概率，提高了用户体验。

附图说明

图 1 为本发明所提供的电子烟的一种实施例整体结构示意图；

20 图 2 为图 1 所示电子烟的剖面结构示意图；

图 3 为本发明所提供的电子烟内的电路连接的一种实施例的结构示意图；

图 4 为图 1 所示电子烟中的雾化模块的一个实施例的剖面结构示意图；

图 5 为图 1 所示电子烟中的语音识别模块的一个实施例的示意图；

图 6 为本发明中电子烟雾化控制方法的一个实施例的流程图。

25 具体实施方式

本发明公开了一种电子烟，能够让用户采用语音在一个电子烟内选择不同口味的烟液。

下面将结合本发明实施例中的附图，对本发明实施例中的技术方案进行清楚、完整地描述，显然，所描述的实施例仅仅是本发明一部分实施例，而不是

-5-

全部的实施例。基于本发明中的实施例，本领域普通技术人员在没有做出创造性劳动前提下所获得的所有其他实施例，都属于本发明保护的范围。

请参阅图 1，图 1 为本发明所提供的电子烟的一种实施例整体结构示意图。

本实施例中，电子烟 100 包括：

- 5 电子烟本体，且所述电子烟本体设置有吸烟端 101，用户通过该吸烟端 101 即可进行吸烟。

所述电子烟本体内还设置雾化模块 102 和电池模块 103。

请参阅图 2 和图 3，图 2 为图 1 所示电子烟的剖面结构示意图，图 3 为本发明所提供的电子烟内的电路连接的一种实施例的结构示意图。

- 10 如图 2 和图 3 所示，所述电子烟本体内还设置有语音识别模块 301，用于接受语音，并根据接收到的语音产生不同的选择信号，其中该不同的选择信号包括第一选择信号或者第二选择信号。

- 所述电子烟本体内的雾化模块 102 内设置有至少两个雾化组件，分别为第一雾化组件 201 和第二雾化组件 203，其中第一雾化组件 201 内设置有第一储油空间 202，第二雾化组件 203 内设置有第二储油空间 204，且第一储油空间 202 和第二储油空间 204 分别装载有不同的烟液。具体地，该第一储油空间 202 内和第二储油空间 204 内分别设置有储油棉。当然，实际运用中，该第一储油空间 202 内和第二储油空间 204 内也可以设置有其他储油介质，在此不作限制。

- 所述电子烟本体内还设置有与所述语音识别模块 301 相连接的微控制器 302。若所述语音识别模块 301 根据接收到的语音产生第一选择信号，则所述微控制器 302 用于根据所述第一选择信号与所述第一雾化组件 201 连通。若所述语音识别模块 301 根据接收到的语音产生第二选择信号，则所述微控制器 302 用于根据所述第二选择信号与所述第二雾化组件 203 连通。

- 当然，实际运用中，电子烟本体内可以设置两个以上的雾化组件。相应地，语音识别模块 301 可以根据接收到的语音产生两个以上的选择信号，其中所产生的选择信号的数量等于雾化组件的数量，且各雾化组件与各选择信号一一对应。或者，还可以是语音识别模块 301 根据接收到的语音所产生的选择信号的数量大于雾化组件的数量，使得多余部分的选择信号分别对应着至少两个雾化

-6-

组件。而微控制器 302 则用于根据该语音识别模块 301 所产生的选择信号与该选择信号所对应的雾化组件相连通。

所述电子烟本体内还设置有用于产生第一脉冲信号的、与所述微控制器 302 相连接的气流感应器 303，该气流感应器在检测到电子烟本体内的烟雾通道中的压强变小时，即用户吸烟时会生成脉冲信号。优选地，气流感应器 303 设置在离吸烟端较近的位置，使得气流感应器 303 的感应用户吸烟动作的灵敏度提高，以使用户更为有效的使用电子烟。

所述电池模块 103 用于给所述微控制器 302、所述气流感应器 303、所述第一雾化组件 201 以及第二雾化组件 203 供电。

10 所述微控制还用于接收气流感应器 303 产生的第一脉冲信号，并根据该第一脉冲信号生成第一控制信号。而与所述微控制相连通的雾化组件则根据该第一控制信号控制该雾化组件内所设置的储油空间内的烟液雾化。

具体举例来说，当语音识别模块 301 根据接收到的语音产生第一选择信号时，微控制器 302 用于根据第一选择信号与第一雾化组件 201 连通。在微控制器 302 接收到来自气流感应器 303 的第一脉冲信号时，所述微控制器 302 还用于产生第一控制信号。而与所述微控制器 302 相连通的第一雾化组件 201 根据该第一控制信号控制第一储油空间内的烟液雾化。

当语音识别模块 301 根据接收到的语音产生第二选择信号时，微控制器 302 用于根据第二选择信号与第二雾化组件 203 连通。在微控制器 302 接收到来自气流感应器 303 的第一脉冲信号时，所述微控制器 302 还用于产生第一控制信号。而与所述微控制器 302 相连通的第二雾化组件 203 根据该第一控制信号控制第二储油空间内的烟液雾化。

优选的，语音识别模块 301 还可以根据接收到的语音产生第三选择信号，而微控制器 302 还用于根据该第三选择信号同时与所述第一雾化组件 201 和所述第二雾化组件 203 连通。在微控制器 302 接收到来自气流感应器 303 的第一脉冲信号时，所述微控制器 302 还用于产生第一控制信号。而与所述微控制器 302 相连通的第一雾化组件 201 根据该第一控制信号控制第一储油空间内的烟液雾化，且与所述微控制器 302 也连通的第二雾化组件 203 也根据该第一控制

-7-

信号控制第二储油空间内的烟液雾化,以使用户能够吸食到由两种不同烟液同时雾化后产生的混合烟雾,给用户第三种口味的烟雾选择。当然,实际运用中,也可以是语音识别模块 301 不产生第三种选择信号。以上仅为举例,并不作限制。

- 5 在该电子烟本体内还形成有用于流通已雾化的烟液的烟雾通道,使得用户通过吸烟端 101 吸食流经该烟雾通道内的烟液。

本发明实施例中,由于电子烟本体中设有至少两种雾化组件,其中不同的雾化组件中设有装载着不同烟液的储油空间,且该电子烟上还设有相互连接的语音识别模块和微控制器,其中该语音识别模块根据接收到不同的语音来发出
10 不同的选择信号,而该微控制器根据该不同的选择信号来选择相对应的雾化组件工作,这样,用户能够在一支电子烟上吸食到不同口味的烟液,避免了用户需携带多支电子烟而造成的不便;另外,用户可以采用语音在一个电子烟内选择不同口味的烟液,选择方式方便快捷,提高了用户体验。

本发明中,电子烟本体内的雾化模块 102 中的各雾化组件有多种结构实现
15 方式。下面结合图 4 对该电子烟的雾化模块的一种具体结构进行详细说明。请参阅图 4,图 4 为图 1 所示电子烟中的雾化模块的一个实施例的剖面结构示意图。雾化模块 102 包括:

还包括第一电热丝组件 401 的第一雾化组件 201 和还包括第二电热丝组件 403 的第二雾化组件 203。

- 20 第一雾化组件 201 的第一电热丝组件 401 用于雾化所述第一储油空间 202 内的烟液。具体地,本实施例中,第一储油空间 202 环绕在中空的第一黄纳管 402 上,且第一黄纳管 402 上开有通孔,该通孔的走向垂直于第一黄纳管 402 的走向,以使得第一电热丝组件 401 能穿过该通孔,与所述第一黄纳管 402 相互固定;同时,该第一电热丝组件 401 的两端还分别插入第一储油空间 202
25 中,以能够将第一储油空间 202 内的烟液雾化。当然,实际运用中,第一雾化组件内的第一储油空间和第一电热丝组件也可以通过其他方式设置,并不局限于以上描述。

第二雾化组件 203 的结构与第一雾化组件 201 相同。或者,实际运用中,

-8-

第二雾化组件 203 的结构与第一雾化组件 201 也可以不相同, 第二雾化组件 203 内的第二储油空间 204 和第二电热丝组件 403 也可以采用其他结构方式。在此不作限制。

5 第一储油空间 202 和第二储油空间 204 平行并排设置在电子烟本体内, 其中第一储油空间 202 的两端分别和第二储油空间 204 的两端相邻, 使得第一雾化组件 201 和第二雾化组件 203 平行并排设置在电子烟本体内, 且该两个雾化组件的一端均与电池模块 103 相邻。

本实施例中, 雾化模块 102 内的各雾化组件采用上述排列方式, 能够使得雾化模块 102 内结构紧凑, 减小电子烟本体的体积。

10 优选地, 本实施例中, 第一雾化组件 201 还包括第一雾化器支架 404, 所述第一储油空间 202 设于所述第一雾化器支架 404 上。所述第一雾化器支架 404 靠近所述电池模块 103 的一端设置有用与与所述电池模块 103 可拆卸连接的第一螺纹段 405。具体地, 该第一螺纹段 405 为外螺纹。相对应地, 电池模块 103 靠近所述第一雾化器支架 404 的一端设有第一匹配螺纹, 所述第一雾化器支架 404 和所述电池模块 103 通过所述第一螺纹段 405 和所述第一匹配螺纹的
15 的配合来可拆卸连接。具体地, 该第一匹配螺纹为内螺纹。当然, 实际运用中, 该第一螺纹段也可以是内螺纹, 该第一匹配螺纹也可以是外螺纹, 在此不作限制。

进一步地, 第一雾化器支架 404 上还在所述第一螺纹段 405 内部固定设置
20 有第一雾化器电极 406。当第一雾化组件 201 和电池模块 103 通过螺纹连接时, 该第一雾化器电极 406 与电池模块 103 中的电池电极相连接, 以使得在微控制器在与第一雾化组件 201 连通时电池模块 103 能够为第一雾化组件 201 供电。

同样地, 第二雾化组件 203 还包括第二雾化器支架 407, 所述第一储油空间 202 设于所述第二雾化器支架 407 上。所述第二雾化器支架 407 靠近所述电
25 池模块 103 的一端设置有用与与所述电池模块 103 可拆卸连接的第二螺纹段 408。具体地, 该第二螺纹段 408 为外螺纹。相对应地, 电池模块 103 靠近所述第二雾化器支架 407 的一端设有第二匹配螺纹, 所述第二雾化器支架 407 和所述电池模块 103 通过所述第二螺纹段 408 和所述第二匹配螺纹的配合来可

-9-

拆卸连接。具体地，该第二匹配螺纹为内螺纹。当然，实际运用中，该第二螺纹段也可以是内螺纹，该第二匹配螺纹也可以是外螺纹，在此不作限制。

进一步地，第二雾化器支架 407 上还在所述第二螺纹段 408 内部固定设置有第二雾化器电极 409。当第二雾化组件 203 和电池模块 103 通过螺纹连接时，
5 该第二雾化器电极 407 与电池模块 103 中的电池电极相连接，以使得在微控制器 302 在与第二雾化组件 203 连通时电池模块 103 能够为第二雾化组件 203 供电。

这样，第一雾化组件和第二雾化组件分别通过螺纹段与电池模块 103 可拆卸地连接，以方便用户更换雾化组件。

10 在上面所描述的各雾化组件中，各雾化组件和所述电池模块之间均通过螺纹连接为例进行说明。实际运用中，各雾化组件和所述电池模块之间也可以采用其他可拆卸的连接方式，例如卡和连接。那么，各个雾化器支架上的连接结构不是螺纹段，而是具有弹性的卡和弹片。当然，上述仅为举例，并不作限制。甚至，各个雾化组件和电池模块之间也可以采用不可拆卸的连接方式，在此不
15 作限制。

本发明中，电子烟本体内的语音识别模块 301 有多种实现方式。下面结合图 5 对该电子烟的语音识别模块 301 的一种具体实现方式进行详细说明。请参阅图 5，图 5 为图 1 所示电子烟中的语音识别模块 301 的一个实施例的示意图。

如图 5 所示，所述语音识别模块 301 包括语音接收器 205（参见图 2）和
20 语音识别单元 501。

所述语音接收器 205 用于接收语音信号，并将接收到的语音信号转换为电信号。例如，该语音接收器可以是话筒。当然，上述举例仅为说明，并不作限制。具体地，语音接收器 205 可位于电池模块 103 背向雾化组件 102 的一端（请参阅图 2），与电池模块 103 中的电池电连接。当然，上述仅为语音接收器 205
25 的位置举例，并不作限制。

所述语音识别单元 501 用于根据所述电信号生成相应的所述第一选择信号或者所述选择第二信号，并将所述选择第一信号或者第二选择信号发送至所述微控制器 302。

-10-

实际运用中,语音识别模块 301 中的语音识别单元 501 在出厂前可以预先设置好各预置电信号与各选择信号的一一对应关系。在使用中,当用户说出相应的语音时,语音接收器接收该语音信号并转为电信号发送至语音识别单元 501。语音识别模块 301 判断该电信号是否为预置电信号,若是,则生成与该电信号相对应的选择信号,若不是,则不生成选择信号。

当然,实际运用中,语音识别单元 501 中与各选择信号所对应的电信号也可以不是由厂家来设定,还可以由用户自己来设定,在此不作限制。

优选地,电子烟本体上还设有用于控制语音识别模块 301 中语音接收器 205 的开启和关闭的按键。下面进行详细描述。

10 请参阅图 2,电子烟本体的电池模块 103 上还设有用于接收用户操作指令的按键 206,与所述按键 206 连接设置有用根据所述操作指令生成启动信号的微触开关 207。且所述微触开关 207 与所述语音接收器 205 电连接,以使所述语音接收器 205 能够根据所述启动信号接受语音信号。

15 采用该种设置方式可避免语音接收器一直处于接收语音信号的状态而导致经常误操作,同时也能够节省使用电池模块中的电池电量。

在本发明的电子烟中,优选地,所述电子烟本体内还设置有低压保护模块 304 (请参见图 3),且所述电子烟本体外表面还设有与所述低压保护模块 304 连接设置的第一提醒装置(图未示)。所述低压保护模块 304 用于控制所述第一提醒装置的工作状态。所述第一提示装置可以为液晶屏,LED 灯或发生器,20 这里不作限定。具体地,第一提示装置为 LED 灯,低压保护模块 304 可在该电子烟的电池电量低于预先设置的阈值时,控制第一提示装置点亮或者以一定频率进行闪烁。

在本发明的电子烟中,优选地,所述电子烟本体内还设置有过流保护模块 305 (请参见图 3);且所述电子烟本体外表面还设有与所述过流保护模块 305 25 连接设置的第二提醒装置(图未示)。所述过流保护模块 305 用于控制所述第二提醒装置的工作状态。所述第二提示装置可以为液晶屏,LED 灯或发生器,这里不作限定。具体地,第二提示装置为 LED 灯,过流保护模块 305 在该电子烟的线路发生短路时,控制第二提示装置点亮或者以一定频率进行闪烁;在

电子烟的线路正常时，控制该第二提示装置熄灭。

上面对本发明实施例中的电子烟进行了描述，下面对本发明实施例中的电子烟雾化控制方法进行描述。请参阅图 6，本发明中电子烟雾化控制方法的一个实施例包括：

5 601、电子烟获取语音信号；

本实施例中，电子烟上设置有语音接收器，可以接受语音信号。而且，电子烟内还设有至少两个雾化组件，其中不同的雾化组件分别连接设置有不同的储油空间，其中不同储油空间上装载有不同的烟液。

10 602、电子烟根据所述语音信号生成不同的选择信号，其中所述不同的选择信号对应着不同的雾化组件；

电子烟可以根据接收到的语音产生两个以上的选择信号，其中所产生的选择信号的数量等于电子烟内所设置的雾化组件的数量，且各雾化组件与各选择信号一一对应。或者，还可以是电子烟根据接收到的语音所产生的选择信号的数量大于电子烟内所设置的雾化组件的数量，使得多余部分的选择信号分别对
15 应着至少两个雾化组件。

本实施例中，并不是所有的语音信号都能让电子烟生成选择信号。电子烟内预先设置好与各选择信号相对应的各预置语音信号，只有当电子烟所接受到的语音信号与其所设置好的各预置语音信号中的一个预置语音信号一致时，电子烟才能根据所接受到的语音信号生成相对应的选择信号，若不一致，则电子
20 烟不生成选择信号。

电子烟内与各选择信号相对应的各预置语音信号可以在电子烟出厂前预先设置好。或者，也可以由用户自己来设定，在此不作限制。

603、电子烟根据所生成的选择信号选定对应的雾化组件；

电子烟内预先设置好与各选择信号所对应的雾化组件。值得注意的是，本
25 实施例中，一个选择信号可以对应着一个雾化组件，也可以对应着至少两个雾化组件。当电子烟根据所接受到的语音信号生成对应的选择信号后，电子烟再根据该生成的选择信号选定与该选择信号相对应的一个或者至少两个雾化组件，即使得这一个或者至少两个雾化组件进入待工作的状态。

-12-

具体举例来说，在电子烟内的电路中，电子烟的每个雾化组件的两个电极中的一个分别与用于供电的电池相连接，而另一个电极与电路断开，处于未连通的状态。当电子烟根据接受到语音信号生成选择信号时，电子烟将该选择信号所对应的雾化组件的与电路断开的电极连通到电路中去，以使得该对应的雾化组件处于待工作的状态。

优选地，电子烟包括第一雾化组件和第二雾化组件；若所述选择信号为第一选择信号，则选定第一雾化组件；若所述电信号为第二选择电信号，则选定第二雾化组件；若所述电信号为第三选择电信号，则同时选定第一雾化组件和第二雾化组件。这样，电子烟内只设置有两种雾化组件却能让用户吸食到三种口味的烟液。

604、电子烟当检测到内部压力变化时，控制所述选定的雾化组件工作；

当用户开始吸食电子烟时，电子烟的内部压力发生变化。而当电子烟检测到内部压力变化时，电子烟控制内部电路开始工作，即控制所选定的雾化组件开始工作，使得该雾化组件内的烟液开始雾化，进而被用户所吸食。

本说明书中各个实施例采用递进的方式描述，每个实施例重点说明的都是与其他实施例的不同之处，各个实施例之间相同相似部分互相参见即可。

对所公开的实施例的上述说明，使本领域专业技术人员能够实现或使用本发明。对这些实施例的多种修改对本领域的专业技术人员来说将是显而易见的，本文中所定义的一般原理可以在不脱离本发明的精神或范围的情况下，在其它实施例中实现。因此，本发明将不会被限制于本文所示的这些实施例，而是要符合与本文所公开的原理和新颖特点相一致的最宽的范围。

+

-13-

权 利 要 求

1、一种电子烟，其特征在于，包括：

电子烟本体；

5 所述电子烟本体设置有吸烟端、用于根据接收到的语音产生不同选择信号的语音识别模块和雾化模块，所述不同选择信号包括第一选择信号或者第二选择信号，所述雾化模块至少包括第一雾化组件和第二雾化组件，所述第一雾化组件内和所述第二雾化组件内分别设置有装载不同烟液的第一储油空间和第二储油空间；

10 与所述语音识别模块相连接的微控制器，用于根据所述第一选择信号与所述第一雾化组件连通，或根据所述第二选择信号与所述第二雾化组件连通；

所述电子烟本体还设置有用于产生第一脉冲信号的、与所述微控制器相连接的气流感应器，和用于给所述微控制器、所述第一雾化组件以及第二雾化组件供电的电池模块；

15 所述微控制器还用于根据所述第一脉冲信号生成第一控制信号，与所述微控制器连通的雾化组件用于根据所述第一控制信号雾化相应的储油空间内的烟液。

2、根据权利要求1所述的电子烟，其特征在于，

所述语音识别模块还用于根据接收到的语音产生第三选择信号；

20 所述微控制器还用于根据所述第三选择信号同时与所述第一雾化组件和所述第二雾化组件连通。

3、根据权利要求1所述的电子烟，其特征在于，

所述第一雾化组件还包括用于雾化所述第一储油空间内的烟液的第一电热丝组件；

25 所述第一雾化组件还包括用于雾化所述第二储油空间内的烟液的第二电热丝组件；

所述第一储油空间的两端分别和所述第二储油空间的两端相邻，以使所述第一储油空间和第二储油空间平行并排设置在所述电子烟本体内。

4、根据权利要求3所述的电子烟，其特征在于，

所述第一雾化组件还包括：

-14-

第一雾化器支架,所述第一雾化器支架靠近所述电池模块的一端设置第一螺纹段,所述电池模块靠近所述第一雾化器支架的一端设有第一匹配螺纹,所述第一雾化器和所述电池模块通过所述第一螺纹段和所述第一匹配螺纹的配合来可拆卸连接;

5 所述第一储油空间设于所述第一雾化器支架上;

所述第二雾化组件还包括:

第二雾化器支架,所述第二雾化器支架靠近所述电池模块的一端设置第二螺纹段,所述电池模块靠近所述第二雾化器支架的一端还设有第二匹配螺纹,所述第二雾化器和所述电池模块通过所述第二螺纹段和所述第二匹配螺纹的

10 配合来可拆卸连接;

所述第二储油空间设于所述第二雾化器支架上。

5、根据权利要求1所述的电子烟,其特征在于,

所述语音识别模块包括语音接收器和语音识别单元;

所述语音接收器用于接收语音信号,并将接收到的语音信号转换为电信

15 号;

所述语音识别单元用于根据所述电信号生成相应的所述第一选择信号或者所述选择第二信号,并将所述选择第一信号或者第二选择信号发送至所述微控制器。

6、根据权利要求5所述的电子烟,其特征在于,所述电池模块还包括:

20 用于接收用户操作指令的按键;

与所述按键连接设置有利于根据所述操作指令生成启动信号的微触开关;

且所述微触开关与所述语音接收器连接,以使所述语音接收器根据所述启动信号接受语音信号。

7、根据权利要求1所述的电子烟,其特征在于,

25 所述电子烟本体内还设置有低压保护模块;

所述电子烟本体外表面还设有与所述低压保护模块连接设置的第一提醒装置;

所述低压保护模块用于控制所述第一提醒装置的工作状态。

8、根据权利要求1所述的电子烟,其特征在于,

—15—

所述电子烟本体内还设置有过流保护模块;

所述电子烟本体外表面还设有与所述过流保护模块连接设置的第二提醒装置;

所述过流保护模块用于控制所述第二提醒装置的工作状态。

5 9、一种电子烟雾化控制方法,其特征在于,包括:

所述电子烟内设有至少两个雾化组件,其中不同的雾化组件分别设置有不同的储油空间,其中不同储油空间上装载有不同的烟液;

所述电子烟获取语音信号;

10 所述电子烟根据所述语音信号生成不同的选择信号,其中所述不同的选择信号对应着所述不同的雾化组件;

所述电子烟根据所生成的选择信号选定对应的雾化组件;

所述电子烟当检测到内部压力变化时,控制所述选定的雾化组件工作。

10、根据权利要求9所述的电子烟雾化控制方法,其特征在于,

所述电子烟包括第一雾化组件和第二雾化组件;

15 所述电子烟根据所生成的选择信号选定对应的雾化组件具体包括:

若所述选择信号为第一选择信号,则选定第一雾化组件;

若所述电信号为第二选择电信号,则选定第二雾化组件;

若所述电信号为第三选择电信号,则同时选定第一雾化组件和第二雾化组件。

20

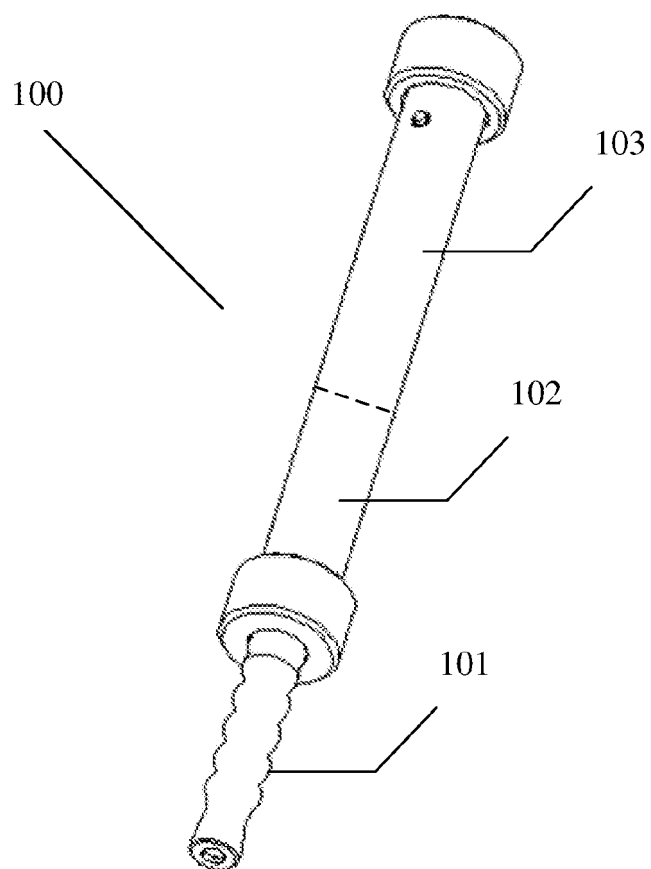


图 1

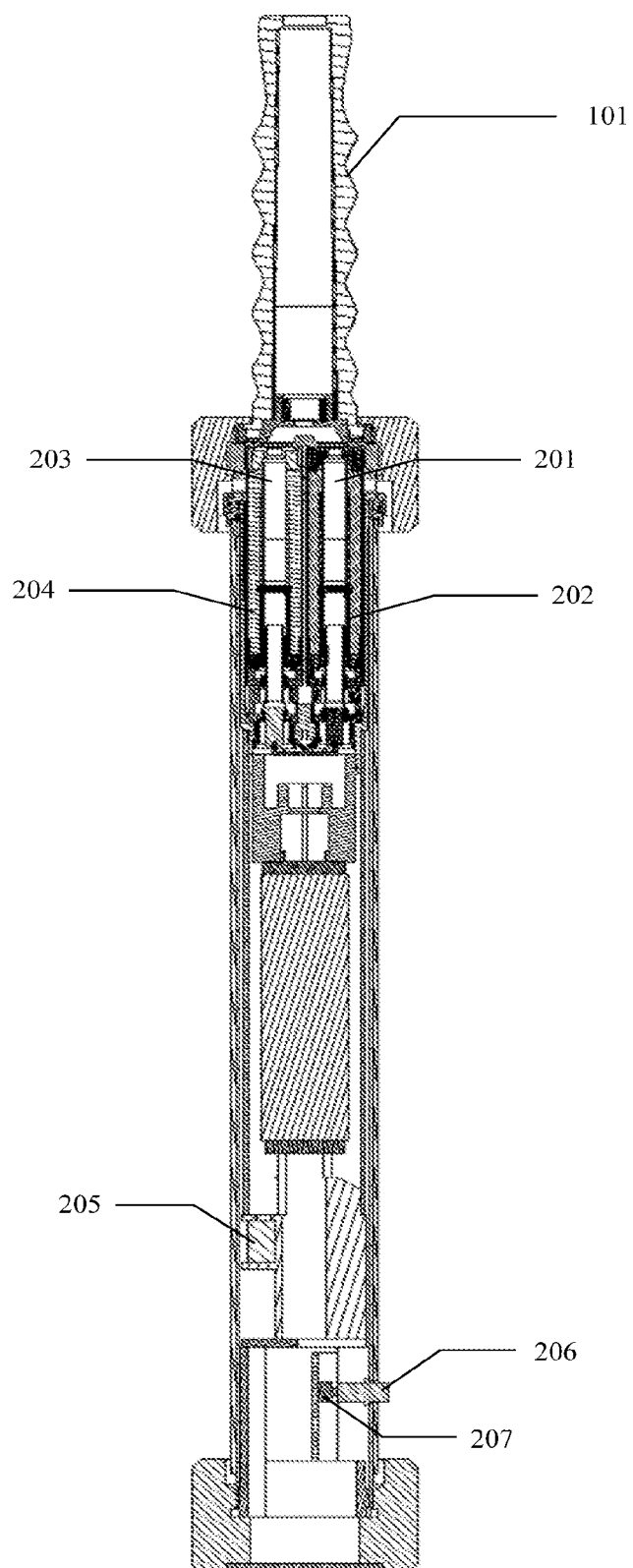


图 2

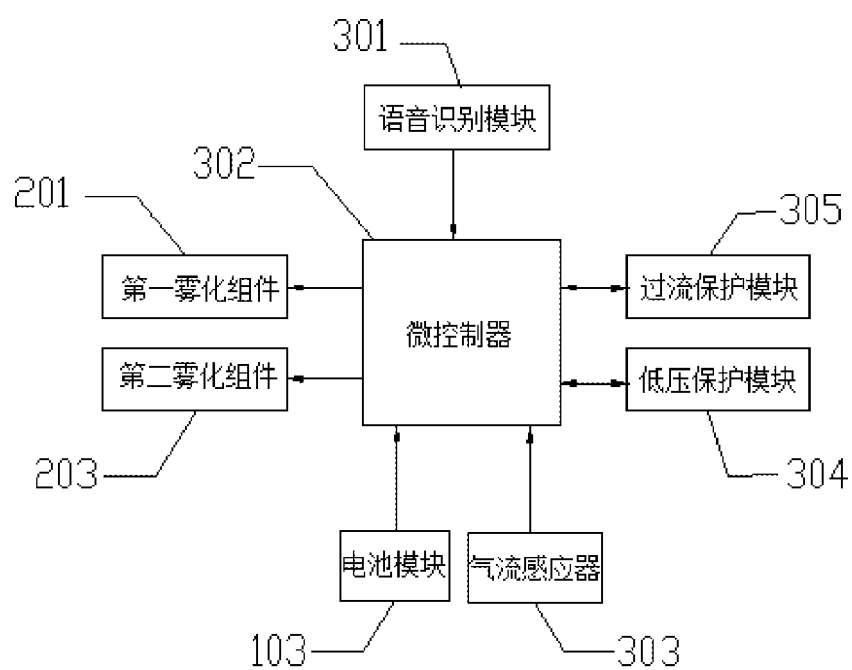


图 3

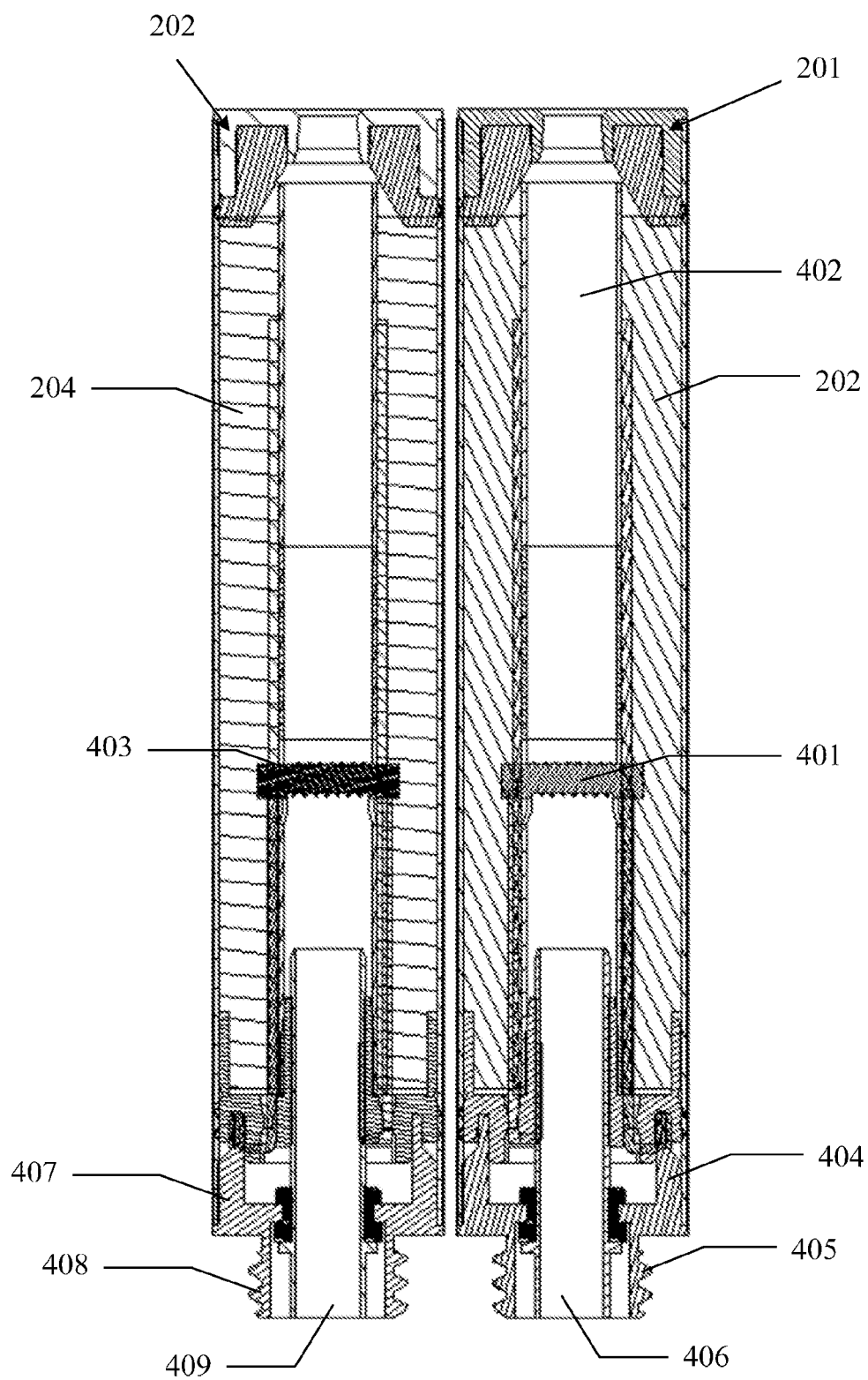


图 4

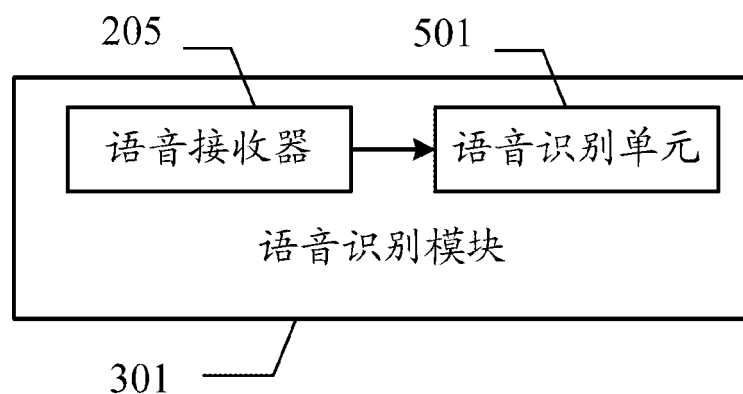


图 5

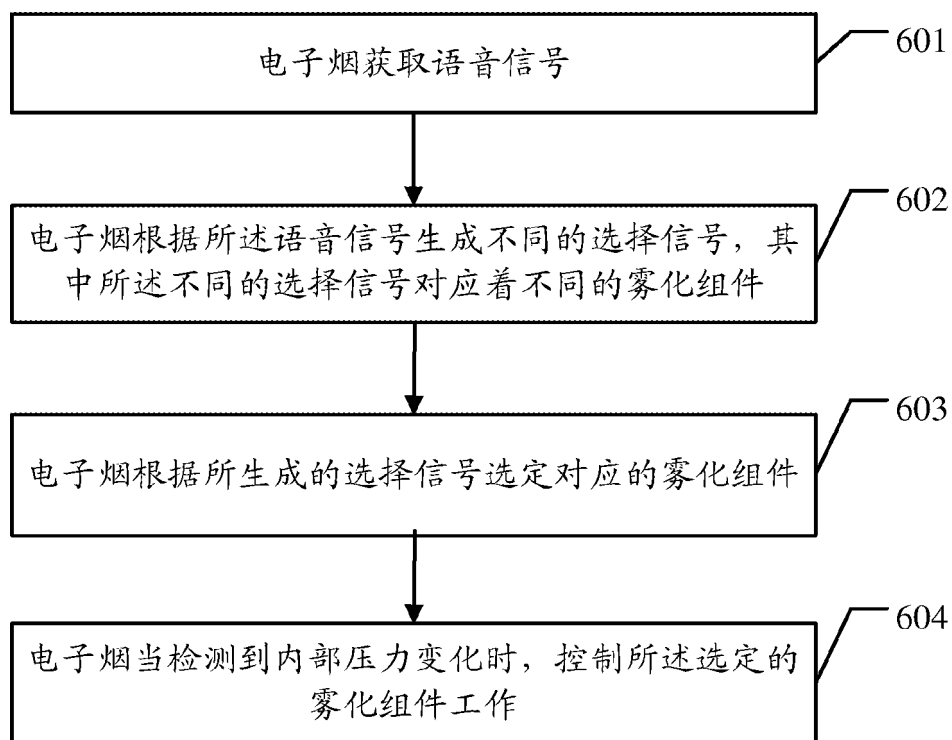


图 6

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2015/075101

A. CLASSIFICATION OF SUBJECT MATTER

A24F 47/00 (2006.01) i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CNABS, CNTXT, EPODOC, WPI, VEN, CNKI, ISI: LIU, Qiuming; KIMREE, different, any, electronic 2d cigarette?, atomiz+, taste+, more, several, multiple?, two, three, double+, sound+, voice+, speech+, audio+, recogni+, identifi+, distinguish+, judg+, choos+, choice?, select+

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	CN 103859609 A (LIU, Qiuming), 18 June 2014 (18.06.2014), claims 1-10	1-10
A	WO 2014032275 A1 (LIU, Qiuming), 06 March 2014 (06.03.2014), description, paragraphs 0028-0047, and figures 1-5	1-10
A	CN 202436108 U (GU, Lou), 19 September 2012 (19.09.2012), the whole document	1-10
A	CN 202445135 U (CHINA TOBACCO HUBEI INDUSTRIAL CO., LTD. et al.), 26 September 2012 (26.09.2012), the whole document	1-10
A	CN 103054196 A (SHENZHEN FIRST UNION TECHNOLOGY CO., LTD.), 24 April 2013 (24.04.2013), the whole document	1-10
A	CN 103519351 A (HONGTA TOBACCO (GROUP) CO., LTD.), 22 January 2014 (22.01.2014), the whole document	1-10

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 02 June 2015 (02.06.2015)	Date of mailing of the international search report 17 June 2015 (17.06.2015)
Name and mailing address of the ISA/CN: State Intellectual Property Office of the P. R. China No. 6, Xitucheng Road, Jimenqiao Haidian District, Beijing 100088, China Facsimile No.: (86-10) 62019451	Authorized officer GENG, Na Telephone No.: (86-10) 62413465

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2015/075101

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2014032276 A1 (LIU, Qiuming), 06 March 2014 (06.03.2014), the whole document	1-10
A	US 2010031968 A1 (GAMUCCI LIMITED), 11 February 2010 (11.02.2010), the whole document	1-10

Form PCT/ISA/210 (continuation of second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2015/075101

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
CN 103859609 A	18 June 2014	None	
WO 2014032275 A1	06 March 2014	KR 20140058507 A	14 May 2014
		US 2014060527 A1	06 March 2014
		JP 2014528717 A	30 October 2014
		CA 2882773 A1	06 March 2014
		EP 2740371 A1	11 June 2014
		CN 203087527 U	31 July 2013
		US 2013340778 A1	26 December 2013
		CN 104023570 A	03 September 2014
		AU 2012388597 A1	16 April 2015
CN 202436108 U	19 September 2012	US 2013168880 A1	04 July 2013
CN 202445135 U	26 September 2012	None	
CN 103054196 A	24 April 2013	US 2014190503 A1	10 July 2014
		EP 2754361 A1	16 July 2014
CN 103519351 A	22 January 2014	None	
WO 2014032276 A1	06 March 2014	CN 104023569 A	03 September 2014
		KR 20140070524 A	10 June 2014
		US 2014060556 A1	06 March 2014
		EP 2732713 A1	21 May 2014
		CA 2882840 A1	06 March 2014
		JP 2014528718 A	30 October 2014
		CN 203087527 U	31 July 2013
		AU 2012388598 A1	16 April 2015
		US 2013340778 A1	26 December 2013
US 2010031968 A1	11 February 2010	GB 2465247 A	19 May 2010
		GB 2465247 B	20 March 2013

Form PCT/ISA/210 (patent family annex) (July 2009)

国际检索报告

国际申请号

PCT/CN2015/075101

A. 主题的分类

A24F 47/00(2006.01)i

按照国际专利分类(IPC)或者同时按照国家分类和IPC两种分类

B. 检索领域

检索的最低限度文献(标明分类系统和分类号)

A24

包含在检索领域中的除最低限度文献以外的检索文献

在国际检索时查阅的电子数据库(数据库的名称, 和使用的检索词(如使用))

CNABS, CNTXT, EPDOC, WPI, VEN, CNKI, ISI:刘秋明, 吉瑞, 电子烟, 雾化, 口味, 味道, 两, 不同, 多, 任意, 双, 语音, 声音, 声, 识别, 判断, 选择, 选取, electronic 2d cigarette?, atomiz+, taste+, more, several, multiple?, two, three, double+, sound+, voice+, speech+, audio+, recogni+, identif+, distinguish+, judg+, choos+, choice?, select+

C. 相关文件

类 型*	引用文件, 必要时, 指明相关段落	相关的权利要求
PX	CN 103859609 A (刘秋明) 2014年 6月 18日 (2014 - 06 - 18) 权利要求1-10	1-10
A	WO 2014032275 A1 (刘秋明) 2014年 3月 6日 (2014 - 03 - 06) 说明书第0028-0047段、附图1-5	1-10
A	CN 202436108 U (顾楼) 2012年 9月 19日 (2012 - 09 - 19) 全文	1-10
A	CN 202445135 U (湖北中烟工业有限责任公司 等) 2012年 9月 26日 (2012 - 09 - 26) 全文	1-10
A	CN 103054196 A (深圳市合元科技有限公司) 2013年 4月 24日 (2013 - 04 - 24) 全文	1-10
A	CN 103519351 A (红塔烟草集团有限责任公司) 2014年 1月 22日 (2014 - 01 - 22) 全文	1-10

☒ 其余文件在C栏的续页中列出。☒ 见同族专利附件。

* 引用文件的具体类型:

“A” 认为不特别相关的表示了现有技术一般状态的文件	“T” 在申请日或优先权日之后公布, 与申请不相抵触, 但为了理解发明之理论或原理的在后文件
“E” 在国际申请日的当天或之后公布的在先申请或专利	“X” 特别相关的文件, 单独考虑该文件, 认定要求保护的发明不是新颖的或不具有创造性
“L” 可能对优先权要求构成怀疑的文件, 或为确定另一篇引用文件的公布日而引用的或者因其他特殊理由而引用的文件(如具体说明的)	“Y” 特别相关的文件, 当该文件与另一篇或者多篇该类文件结合并且这种结合对于本领域技术人员为显而易见时, 要求保护的发明不具有创造性
“O” 涉及口头公开、使用、展览或其他方式公开的文件	“&” 同族专利的文件
“P” 公布日先于国际申请日但迟于所要求的优先权日的文件	

国际检索实际完成的日期

2015年 6月 2日

国际检索报告邮寄日期

2015年 6月 17日

ISA/CN的名称和邮寄地址

中华人民共和国国家知识产权局(ISA/CN)
北京市海淀区蓟门桥西土城路6号
100088 中国

传真号 (86-10)62019451

受权官员

耿娜

电话号码 (86-10)62413465

表 PCT/ISA/210 (第2页) (2009年7月)

C. 相关文件		
类 型*	引用文件，必要时，指明相关段落	相关的权利要求
A	WO 2014032276 A1 (刘秋明) 2014年 3月 6日 (2014 - 03 - 06) 全文	1-10
A	US 2010031968 A1 (GAMUCCI LIMITED) 2010年 2月 11日 (2010 - 02 - 11) 全文	1-10

表 PCT/ISA/210 (第2页) (2009年7月)

国际检索报告
关于同族专利的信息

国际申请号

PCT/CN2015/075101

检索报告引用的专利文件			公布日 (年/月/日)	同族专利	公布日 (年/月/日)
CN	103859609	A	2014年 6月 18日	无	
WO	2014032275	A1	2014年 3月 6日	KR	20140058507 A 2014年 5月 14日
				US	2014060527 A1 2014年 3月 6日
				JP	2014528717 A 2014年 10月 30日
				CA	2882773 A1 2014年 3月 6日
				EP	2740371 A1 2014年 6月 11日
				CN	203087527 U 2013年 7月 31日
				US	2013340778 A1 2013年 12月 26日
				CN	104023570 A 2014年 9月 3日
				AU	2012388597 A1 2015年 4月 16日
CN	202436108	U	2012年 9月 19日	US	2013168880 A1 2013年 7月 4日
CN	202445135	U	2012年 9月 26日	无	
CN	103054196	A	2013年 4月 24日	US	2014190503 A1 2014年 7月 10日
				EP	2754361 A1 2014年 7月 16日
CN	103519351	A	2014年 1月 22日	无	
WO	2014032276	A1	2014年 3月 6日	CN	104023569 A 2014年 9月 3日
				KR	20140070524 A 2014年 6月 10日
				US	2014060556 A1 2014年 3月 6日
				EP	2732713 A1 2014年 5月 21日
				CA	2882840 A1 2014年 3月 6日
				JP	2014528718 A 2014年 10月 30日
				CN	203087527 U 2013年 7月 31日
				AU	2012388598 A1 2015年 4月 16日
				US	2013340778 A1 2013年 12月 26日
US	2010031968	A1	2010年 2月 11日	GB	2465247 A 2010年 5月 19日
				GB	2465247 B 2013年 3月 20日

表 PCT/ISA/210 (同族专利附件) (2009年7月)

Bibliographic data: WO2015149647 (A1) — 2015-10-08

ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREOF

Page bookmark WO2015149647 (A1) - ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREOF

Inventor(s): LIU QIUMING [CN] $\pm$ (LIU, QIUMING)

Applicant(s): KIMREE HI TECH INC; LIU QIUMING [CN] $\pm$ (KIMREE HI-TECH INC, ; LIU, QIUMING)

Classification: - international: A24F47/00
- cooperative: A24F47/008

Application number: WO2015CN75101 20150326

Priority number(s): CN20141133757 20140403

Also published as: CN103859609 (A) CN103859609 (B)

Abstract of WO2015149647 (A1)

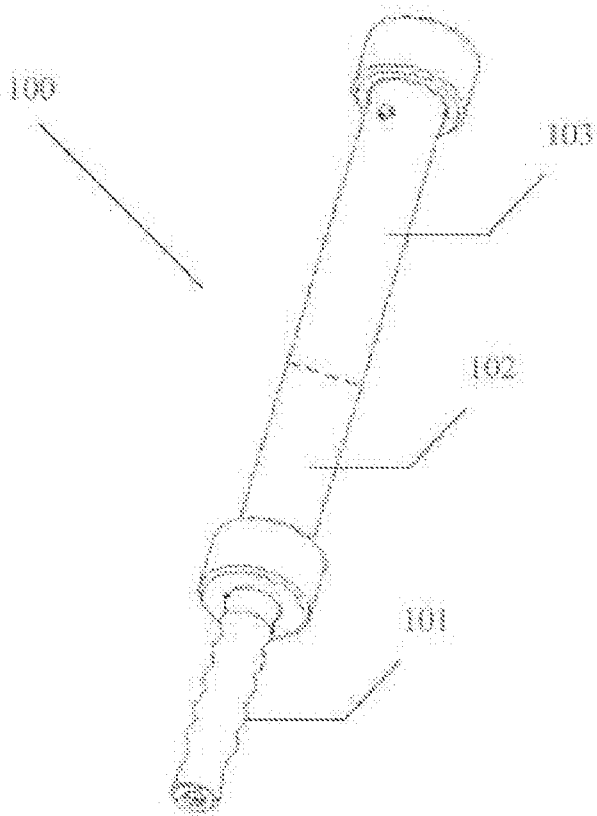


FIG. 4

An electronic cigarette (100) and atomization control method thereof; the electronic cigarette (100) comprises a smoking end (101), a voice recognition module (301) generating different selection signals according to a received voice, an atomization module (102), a microcontroller (302) connected to the voice recognition module (301), an air flow sensor (303), and a battery module (103); the different selection signals comprise a first selection signal or a second selection signal; the atomization module (102) comprises a first atomization assembly (201) and a second atomization assembly (203), and a first oil storage space (202) and a second oil storage space (204) filled with different types of tobacco liquid; the microcontroller (302) is used to communicate with the first atomization assembly (201) according to the first selection signal, or to communicate with the second atomization assembly (203) according to the second selection signal; the air flow sensor (303) is used to generate a first pulse signal, and is connected to the microcontroller (302); and the microcontroller (302) is also used to generate a first control signal according to the first pulse signal, and the atomization assemblies (201, 203) communicating with the microcontroller (302) are used to atomize the tobacco liquid in the corresponding oil storage spaces (202, 204) according to the first control signal. The electronic cigarette (100) enables a user to select by voice different tastes of tobacco liquid in one electronic cigarette (100).

(12) 按照专利合作条约所公布的国际申请

(19) 世界知识产权组织
国际局

(43) 国际公布日
2015 年 11 月 12 日 (12.11.2015)



(10) 国际公布号
WO 2015/168828 A1

(51) 国际专利分类号:
A24F 47/00 (2006.01)

(21) 国际申请号: PCT/CN2014/076715

(22) 国际申请日: 2014 年 5 月 4 日 (04.05.2014)

(25) 申请语言: 中文

(26) 公布语言: 中文

(71) 申请人: 吉瑞高新科技股份有限公司 (KIMREE HI-TECH INC.); 英属维尔京群岛托拉托岛罗德城奎兹天空大厦邮箱 905 号, Tortola (VG)。

(72) 发明人: 刘秋明 (LIU, Qiuming); 中国广东省深圳市宝安区西乡兴业路缤纷世界花园 E3 栋 1202, Guangdong 518000 (CN)。

(74) 代理人: 深圳市顺天达专利商标代理有限公司 (SHENZHEN STANDARD PATENT & TRADE-MARK AGENT LTD.); 中国广东省深圳市福田区深南大道 1056 号银座国际大厦 810-815 室, Guangdong 518040 (CN)。

(81) 指定国 (除另有指明, 要求每一种可提供的国家保护): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW。

(84) 指定国 (除另有指明, 要求每一种可提供的地区保护): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), 欧亚 (AM, AZ, BY, KG, KZ, RU, TJ, TM), 欧洲 (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG)。

本国际公布:

— 包括国际检索报告 (条约第 21 条(3))。

(54) Title: ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREFOR

(54) 发明名称: 电子烟及其雾化控制方法

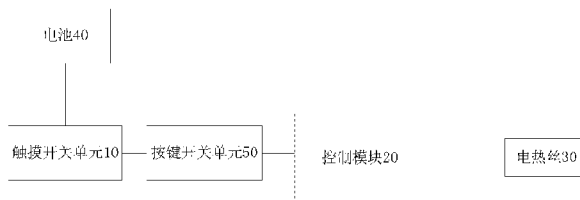


图 2 /FIG. 2

10 Touch switch unit
20 Control module

30 Heating wire
40 Battery
50 Button switch unit

(57) Abstract: An electronic cigarette and an atomization control method therefor. The electronic cigarette comprises an electronic cigarette body. The electronic cigarette body is provided with an atomizer (1) and a battery rod (2). A conductive surface is provided on an outer circumferential face of the electronic cigarette body. The electronic cigarette also comprises a touch switch unit (10) which is electronically connected to the conductive surface, a button switch unit (50) which is connected to the touch switch unit (10) in series, and a control module (20) which is connected to the button switch unit (50); the touch switch unit (10) is used to output a control signal to the button switch unit (50) when a user touches the conductive surface; the button switch unit (50) is used to transmit the control signal to the control module (20) when being started; and the control module (20) is used to control the atomizer (1) according to the received control signal, so as to realize the atomization of the tobacco tar of the electronic cigarette. Beneficial effects: the electronic cigarette is controlled by way of combining the touch switch unit and the button switch unit, so that a heating wire does not generate heat even if the button switch is mis-triggered due to the electronic cigarette being squeezed or knocked, and the security performance is high.

(57) 摘要:

[见续页]

WO 2015/168828 A1



一种电子烟及其雾化控制方法。电子烟包括电子烟本体，电子烟本体设置有雾化器（1）及电池杆（2），电子烟本体的外周面上设置有导电表面，电子烟还包括电连接导电表面的触摸开关单元（10）、与触摸开关单元（10）串联连接的按键开关单元（50）、以及与按键开关单元（50）连接的控制模块（20）；触摸开关单元（10）用于在用户接触导电表面时输出一控制信号至按键开关单元（50）；按键开关单元（50）用于在开启时将控制信号传送给控制模块（20）；控制模块（20）用于根据接收到的控制信号对雾化器（1）进行控制，实现对电子烟的烟油进行雾化。有益效果：采用触摸开关单元结合按键开关单元的方式来实现对电子烟的控制，即使电子烟因挤压或碰撞造成按键开关被误触发，电热丝也不会发热，安全性能高。

说明书

发明名称：电子烟及其雾化控制方法

技术领域

- [1] 本发明涉及电子烟领域，更具体地说，涉及一种电子烟及其雾化控制方法。

背景技术

- [2] 电子烟利用对烟液进行加热产生雾化，给吸烟者提供一种香烟的替代品。
- [3] 目前大多数电子烟通过一个按键开关来控制雾化器工作，如图 1 所示，只需按下按键开关，控制模块便可控制雾化器中的电热丝工作，以加热油烟使其发出烟雾。
- [4] 由于采用了上述按键开关控制方法，电子烟可能会在运输过程中或生活中被乱堆乱放，产品很容易受到挤压碰撞等外界环境因素造成按键开关触发，电热丝发热，从而会带来安全隐患。
- [5] 故现有技术存在缺陷，需要改进。

发明内容

- [6] 本发明要解决的技术问题在于，针对现有技术的上述缺陷，提供一种电子烟及其雾化控制方法。
- [7] 本发明解决其技术问题所采用的技术方案是：构造一种电子烟，包括电子烟本体，所述电子烟本体设置有用于雾化烟油的雾化器以及用于为雾化器提供电源的电池杆，所述电子烟本体的外周面上设置有导电表面，该电子烟还包括电连接所述导电表面的触摸开关单元、与所述触摸开关单元串联连接的按键开关单元、以及与所述按键开关单元连接的控制模块；
- [8] 所述触摸开关单元用于在用户接触所述导电表面时输出一控制信号至所述按键开关单元；
- [9] 所述按键开关单元用于在开启时将该控制信号传送给所述控制模块；
- [10] 所述控制模块用于根据接收到的控制信号对所述雾化器进行控制，实现对电子烟的烟油进行雾化。
- [11] 在上述电子烟中，所述电子烟的吸烟端包覆有导电纸，所述导电纸的表面为

所述导电表面。

- [12] 在上述电子烟中，所述按键开关单元包括按键开关；所述雾化器包括与所述控制模块连接，且用于加热油烟使其发出烟雾的电热丝。
- [13] 在上述电子烟中，所述触摸开关单元包括电连接所述导电表面的触摸感应开关以及与所述触摸感应开关连接的感应信号处理模块；
- [14] 所述触摸感应开关用于在用户接触所述导电表面时发送感应信号给所述感应信号处理模块；
- [15] 所述感应信号处理模块用于对接收的所述感应信号进行放大处理并输出控制信号，在所述按键开关被按下时将该控制信号经所述按键开关传送给所述控制模块。
- [16] 在上述电子烟中，所述触摸感应开关为电连接所述导电表面的感应电容。
- [17] 在上述电子烟中，所述感应信号处理模块由TTP224芯片实现。
- [18] 在上述电子烟中，所述感应信号处理模块的第'1'引脚与所述感应电容连接，所述感应信号处理模块的第'10'引脚分别连接所述电池的正接线端和第一电阻的一端，所述电池的负接线端接地，所述感应信号处理模块的第'16'引脚和所述第一电阻的另一端均与所述按键开关的一端连接，所述按键开关的另一端与所述控制模块连接。
- [19] 在上述电子烟中，所述控制模块的输入引脚与所述按键开关连接，所述控制模块的电源引脚分别与所述电池的正接线端和第一电容的一端连接，所述第一电容的另一端与电池的负接线端连接，所述控制模块的输出引脚和与所述电热丝连接。
- [20] 在上述电子烟中，所述触摸开关单元包括第二电阻以及开关管，所述电池的正接线端电连接所述导电表面，所述开关管的基极电连接设在所述导电表面上的按键开关的顶部金属帽，所述开关管的集电极分别与所述第二电阻的一端和所述按键开关的一端连接，所述第二电阻的另一端与所述电池的正接线端连接，所述开关管的发射极接地，所述按键开关的另一端与所述控制模块连接。
- [21] 在上述电子烟中，所述触摸开关单元还包括连接在所述按键开关的顶部金属帽和所述开关管的基极之间的第四电阻以及连接在所述电池的正接线端和所述

开关管的基极之间的第三电阻。

- [22] 在上述电子烟中，所述触摸开关单元包括运算放大器以及第五电阻，所述运算放大器的反相输入端电连接设在所述导电表面上的所述按键开关的顶部金属帽，所述电池的正接线端连接所述导电表面，所述运算放大器的同相输入端与所述电池的负接线端连接，所述运算放大器的输出端分别与所述第五电阻的一端和所述按键开关的一端连接，所述第五电阻的另一端与所述电池的正接线端连接，所述按键开关的另一端与所述控制模块连接。
- [23] 还提供一种电子烟雾化控制方法，包括：
- [24] 电连接至电子烟本体外周面的导电表面的触摸开关单元检测到用户的触摸动作后输出一控制信号；
- [25] 与所述触摸开关单元电连接的按键开关单元在开启后将所述控制信号传送给所述控制模块；
- [26] 所述控制模块根据接收到的控制信号控制电子烟的雾化器进行雾化烟油。
- [27] 在上述电子烟雾化控制方法中，所述按键开关单元包括按键开关；所述雾化器包括与所述控制模块连接，且用于加热油烟使其发出烟雾的电热丝。
- [28] 在上述电子烟雾化控制方法中，所述触摸开关单元包括电连接所述导电表面的触摸感应开关以及和所述触摸感应开关连接的感应信号处理模块，所述控制方法具体包括：
- [29] 当用户接触所述导电表面并按下所述按键开关时，所述触摸感应开关产生感应信号并将该感应信号发送至所述感应信号处理模块，所述感应信号处理模块将该感应信号进行放大处理，并输出一低电平信号给所述按键开关的一端；
- [30] 此时所述按键开关已闭合，该低电平信号经按键开关的另一端传送给所述控制模块；
- [31] 所述控制模块接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。
- [32] 在上述电子烟雾化控制方法中，所述触摸开关单元包括第二电阻、第三电阻、第四电阻以及开关管，所述电池的正接线端电连接所述导电表面，所述第四电阻连接设在所述导电表面上的所述按键开关的顶部金属帽，所述控制方法

具体包括：

- [33] 当用户握住所述导电表面并按下所述按键开关时，所述导电表面上的电池电压通过肌肤导电传送给所述按键开关的顶部金属帽，并经所述第四电阻传送到所述开关管的基极，所述开关管导通，输出低电平信号给所述按键开关的一端；
- [34] 此时所述按键开关已闭合，该低电平信号经所述按键开关的另一端传送到所述控制模块；
- [35] 所述控制模块接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。
- [36] 在上述电子烟雾化控制方法中，所述触摸开关单元包括运算放大器以及第五电阻，所述运算放大器的反相输入端连接设在所述导电表面上的所述按键开关的顶部金属帽，所述电池的正接线端电连接所述导电表面，所述控制方法具体包括：
- [37] 当用户握住所述导电表面并按下所述按键开关时，所述导电表面上的电池电压通过肌肤导电经所述按键开关的顶部金属帽传送到所述运算放大器的反相输入端，所述运算放大器输出低电平信号给所述按键开关的一端；
- [38] 此时按键开关已闭合，该低电平信号经所述按键开关的另一端传送到所述控制模块；
- [39] 所述控制模块接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。
- [40] 实施本发明的电子烟及其控制方法，具有以下有益效果：通过触摸开关单元结合按键开关单元来实现对电子烟的控制，其中，按键开关单元包括按键开关，电子烟在运输过程中或生活中乱堆乱放的时候，只要用户不需使用电子烟，也就不会接触电子烟本体外周面的导电表面，即使电子烟因挤压或碰撞造成按键开关被误触发，电热丝也不会发热，电子烟不工作，也就不存在安全隐患。有效解决了现有的按键开关经常被误触发时电子烟即可工作，从而导致电子烟发热频率高，缩短电子烟的寿命，电全性能低等问题。

附图说明

- [41] 图 1 是现有的电子烟的 原理框 图；
- [42] 图2是本发明电子烟实施例的 原理框 图；
- [43] 图 3 是 本发明电子烟第一优选实施例的 原理框 图；
- [44] 图 4 是图3中电子烟的电路示意图；
- [45] 图5是本发明电子烟 的结构示意图；
- [46] 图6是本发明电子烟 第二优选实施例的电路示意图；
- [47] 图 7 是本发明电子烟第三优选实施例的电路示意图。

具体实施方式

- [48] 为了对本发明的技术特征、目的和效果有更加清楚的理解，现对照附图详细说明本发明的具体实施方式。
- [49] 本发明实施例的电子烟及电子烟 雾化 控制方法，通过增加一 电连接电子烟本体导电表面 的触摸开关单元，当用户抽烟时用手触摸电池杆或握住电池杆（常规手拿电子烟即可），此时触摸开关单元输出一控制信号，在按下按键开关后该控制信号经按键开关传送给控制模块，才可控制电热丝工作，即控制电子烟正常工作。因此电子烟正常工作必须通过 用户接触电子烟导电表面 加按键开关控制，两者缺一则电子烟不工作，避免了用户携带电子烟时按键开关可能被误触发而造成危害。
- [50] 如图2所示，为本发明电子烟实施例的 原理框 图。可以理解的是，电子烟包括电子烟本体，电子烟本体设置有 用于雾化烟油的雾化器和用于为雾化器提供电源的电池杆，特别地，在本实施例中，电子烟本体的外周面上设置为导电表面，其中，电子烟的吸烟端也可包覆导电纸，导电纸的表面为导电表面。本发明实施例的电子烟 具体 包括：触摸开关单元10、按键开关单元50、控制模块20以及电热丝30。其中，电热丝30为雾化器的加热装置，触摸开关单元10连接 电子烟本体 的 导电表面，触摸开关单元10和按键开关单元50串联连接，按键开关单元50、控制模块20以及电热丝30依次连接。当用户接触 电子烟导电表面 时，触摸开关单元10会输出一控制信号，同时在按键开关单元50接通后，该控制信号会经按键开关单元50传送给控制模块20，控制模块20在接收到该控制信号后，根据该控制信号控制输出电压给电热丝30供电，即控制电热丝30发热。电热丝3

0为雾化器加热装置，用于加热电子烟内部烟油使其发出烟雾，电子烟正常工作。因此在该实施例中，通过采用触摸开关单元10结合按键开关单元50的方式实现对电子烟的雾化控制，可有效解决现有的按键开关经常被误触发时电子烟即可工作，从而导致电子烟发热频率高，缩短电子烟的寿命，安全性能低等问题。

- [51] 如图2所示，为本发明电子烟第一优选实施例的原理框图。在该实施例中，电子烟的导电表面上设有触摸感应区，结合图1，上述触摸开关单元10包括连接电子烟导电表面的触摸感应开关101，按键开关单元50包括按键开关K1，可以理解的是，该触摸感应开关101位于电子烟导电表面上的触摸感应区；按键开关单元50可以为按键开关，也可作为其它开关如触摸感应开关等，在此不作限制，在本实施例中以按键开关为例。触摸感应开关101是一种电子开关，无接触压力、无机械式触点结构；通过检测用户接近或触摸感应区引起物理变化量（如电容值、电阻值等），继而转化为电开关信号。
- [52] 上述触摸开关单元10还包括与触摸感应开关101连接的感应信号处理模块102，当用户接触电子烟导电表面时（包括用手触摸电池杆导电表面或用户吸烟时口腔接触电子烟吸烟端的导电表面），触摸感应开关101发送感应信号（电开关信号）给感应信号处理模块102，感应信号处理模块102将接收到的感应信号进行放大处理，并输出一控制信号，同时在按下按键开关K1后，该控制信号才能经按键开关发送给控制模块20，控制模块20再根据这一控制信号对电热丝进行控制，实现对电子烟的烟油进行雾化，电子烟正常工作。
- [53] 在本实施例中，电子烟还包括电池供电模块（图未示），用于给电池40充电和供电以及给电子烟整个电路提供各种所需电压。
- [54] 如图3所示，为图2中电子烟的电路示意图。在该实施例中，上述触摸感应开关101优选为电容式感应，即该触摸感应开关101为连接电子烟导电表面的电容C，感应信号处理模块102在本实施例中优选为以TTP224芯片实现。具体地，电容C的一端连接电子烟的导电表面，电容C的另一端与感应信号处理模块102的第'1'引脚连接，该引脚为输入引脚，接入感应信号，感应信号处理模块102的第'10'引脚分别连接电池的正接线端B+和电阻R1的一端，该引脚为电源引脚

，电池通过该引脚给信号处理模块102供电，电池的负接线端B-接地，感应信号处理模块102的第'16'引脚和电阻R1的另一端均与按键开关K1的一端连接，该引脚为感应信号处理模块的输出引脚，即根据输入引脚接收的感应信号输出一控制信号，按键开关K1的另一端与控制模块20连接。

[55] 在本实施例中，控制模块20优选为由常用的电子烟管理IC如S080或者CT833实现，在本实施例中优选为型号是S080的微处理器。其中：控制模块20的输入引脚连接按键开关K1，该引脚用于接收按键开关K1所传送的控制信号。控制模块20的电源引脚分别连接电池的正接线端B+和经电容C1连接至电池的负接线端B-，控制模块20的输出引脚与电热丝30连接，该引脚用于根据输入引脚所接收到的控制信号输出电压给电热丝30。控制模块20的另一输出引脚连接至少两个并联二极管的阳极公共端，该至少两个并联二极管的阴极公共端接地，在本实施例中优选为两个并联发光二极管D1和D2，分别用于提示抽烟状态以及电池充电状态。

[56] 结合图2和图3，现详细介绍本发明电子烟第一优选实施例的工作原理如下：当用户用手触摸到或吸烟时口腔接触到电子烟的导电表面所对应的触摸感应区域时，会引起感应电容C的值发生变化，即产生感应信号，这一感应信号传送到感应信号处理模块的第'1'引脚，即输入端口，感应信号处理模块在接收到该感应信号后对该感应信号进行处理，并在第'16'引脚输出一低电平信号（即控制信号）给按键开关K1；同时按下按键开关K1，感应信号处理模块输出的低电平信号经该按键开关传送给控制模块的输入引脚，该引脚为低电平有效，即在输入引脚接收到低电平信号后，该控制模块在第二输出引脚会输出电压给雾化器内的电热丝进行供电，而电热丝为雾化器加热装置，用于加热烟油使雾化组件发出烟雾，电子烟正常工作。

[57] 在上述过程中，若用户不使用电子烟，即不会接触电子烟的导电表面，此时感应信号处理模块的第'1'引脚就接收不到感应信号，其第'16'引脚电平为高电平，此时即使按下按键开关，控制模块的输入引脚电平也为高电平，而该引脚为低电平有效，因此控制模块不能被触发，即在输出引脚不会输出电压给电热丝进行供电，电子烟不工作，因此需使电子烟正常工作，必须满足两个

条件：用户接触电子烟的导电表面以及按下按键开关，只有满足这两个条件电热丝才能发热，以加热烟油使雾化器发出烟雾，电子烟正常工作。在生活中因经常将电子烟乱丢乱放等很容易对电子烟造成挤压或碰撞，易使按键开关误触发，通过采用本实施例提供的电子烟，即使按键开关被误触发，只要用户不使用电子烟，也就不会接触电池杆，控制模块就不会输出电压给电热丝供电，电子烟便不能正常工作，不存在安全隐患。

[58] 如图5所示，为本发明电子烟的结构示意图，该电子烟本体包括雾化器1和电池杆2，雾化器1包括电热丝30。结合图5及图6，在本实施例中，上述触摸开关单元10包括电阻R2、电阻R3、电阻R4以及开关管Q1，在本实施例中，开关管Q1优选为NPN型三极管，电池40的正接线端B+连接电池杆的导电表面，电阻R4的一端连接设在电池杆的导电表面上的按键开关K1的顶部金属帽J1上，电阻R4的另一端与开关管Q1的基极连接，电阻R3的一端和电阻R2的一端均与电池的正接线端B+连接，电阻R3的另一端与开关管Q1的基极连接，电阻R2的另一端分别与开关管Q1的集电极和按键开关K1的一端连接，开关管Q1的发射极接地。此外，按键开关K1的另一端接入控制模块20，控制模块20与电热丝30连接。在本实施例中，按键开关K1、控制模块20、电热丝30及一些元器件如发光二极管等的连接关系与图4是完全相同的，在此不再赘述。

[59] 参见图5及图6，现详细介绍本发明电子烟第二优选实施例的工作原理如下：当用户手握电池杆（手触摸区域覆盖连接电池正接线端B+的电池杆导电表面以及按键开关顶部金属帽）时，因电池杆的导电表面与电池的正接线端B+连接，此时电池电压通过肌肤导电传送到按键开关的顶部金属帽J1（可以理解的是，按键开关顶部金属帽是设在电池杆的导电表面上的），因此按键开关顶部金属帽J1上的电压为电池电压，其经电阻R4加至三极管Q1的基极，此时三极管Q1的基极电平为高电平，而三极管Q1的发射极接地，此时三极管Q1的基极与发射极间的电压大于其导通电压，三极管Q1处于饱和导通状态，三极管Q1的集电极与发射极直通，因此三极管Q1的集电极电平为低电平。

[60] 同时再按下按键开关K1，控制模块20的输入引脚电平（图中为第4'引脚）为

低电平（低电平有效），此时控制模块20的输出引脚（图中为第'8'引脚）会输出电压给电热丝30供电，加热烟油使其产生烟雾，电子烟正常工作。

- [61] 在上述过程中，若用户不需使用电子烟、电子烟被隔置在一旁时，用户不会特意触摸或握住电池杆的导电表面，此时电池电压不会经正接线端B+传送到按键顶部金属帽J1，J1悬空，三极管Q1的基极电平为低电平，不足以导通，而三极管Q1的集电极经电阻R2与电池的正接线端B+连接，因此三极管Q1的集电极电平为高电平，此时即使按下按键开关K1，按键开关K1两端电位相同，控制模块20的输入引脚也为高电平，而该引脚为输入低电平有效，此时控制模块20的输出引脚不会输出电压给电热丝30，即不能控制电热丝30发热，即电子烟不工作。因此该实施例也很好的实现了只要用户不需使用电子烟，也就不会握住电池杆，即使按键开关K1被误触发，电热丝也不会发热，电子烟不工作，也就不存在安全隐患。
- [62] 如图7所示，为本发明电子烟第三优选实施例的电路示意图。结合图2，在该实施例中，触摸开关单元10包括运算放大器U1以及电阻R5，运算放大器U1的反相输入端连接设在电池杆的导电表面上的按键开关的顶部金属帽上，电池40的正接线端B+连接电池杆的导电表面，运算放大器U1的同相输入端与电池的负接线端B-连接，运算放大器U1的输出端分别与电阻R5的一端和按键开关K1的一端连接，电阻R5的另一端电池的正接线端B+连接，按键开关K1的另一端接入控制模块20。在本实施例中，按键开关K1、控制模块20、电热丝30及一些元器件如发光二极管等的连接关系与图4是完全相同的，在此不再赘述。
- [63] 参见图5及图7，现详细介绍本发明第三优选实施例的工作原理如下：当用户手握住电池杆（手指触摸区域覆盖连接电池正接线端B+的电池杆的导电表面以及按键顶部金属帽）时，因电池杆的导电表面与电池的正接线端B+连接，此时电池电压通过肌肤导电传送到按键开关的按键顶部金属帽J1，因此按键开关顶部金属帽J1上的电压为电池电压，因其设有运算放大器U1的反相输入端，而运算放大器U1的同相输入端接地，即该运算放大器的反相输入端电压高于同相输入端电压，因此运算放大器的输出端输出低电平。
- [64] 同时按下按键开关K1，控制模块20的输入引脚为低电平（该引脚为低电平有效

），此时控制模块20的输出引脚会输出电压给电热丝30供电，加热烟油使其产生烟雾，电子烟可正常工作。

- [65] 在上述过程中，当用户不使用电子烟、电子烟被隔置在一旁时，用户不会特意触摸或握住电池杆，此时电池电压不会经正接线端B+传送到按键顶部金属帽J1，J1悬空，运算放大器U1的反相输入端电平为低电平，因运算放大器U1的输出端经电阻R5连接至电池的正接线端B+，即运算放大器的输出电平为高电平，此时即使按下按键开关K1，按键开关K1两端电位相同，控制模块20的输入引脚也为高电平（该引脚为低电平有效），因此控制模块20不会输出电压给电热丝30供电，即电热丝30不发热，电子烟不工作。因此该实施例也很好的实现了即使按键开关K1被误触发，只要用户没有触摸电池杆的金属外壳，电热丝就不会发热，不存在安全隐患。
- [66] 本发明还提供了一种电子烟雾化控制方法，该电子烟包括电子烟本体，电子烟本体又包括雾化器1和电池杆2，雾化器2包括电热丝30，电池杆2包括电池40，特别地，该电子烟本体的外周面上设置有导电表面，该电子烟本体还包括连接电子烟电池杆导电表面的触摸开关单元10、与触摸开关单元10串联连接的按键开关单元50、以及与按键开关单元50连接的控制模块20，该控制方法包括：
- [67] 当用户接触电池杆，触摸开关单元10检测到用户的触摸动作后输出一控制信号；
- [68] 开启按键开关单元50，该控制信号经按键开关单元50传送给控制模块20；
- [69] 控制模块20接收到该控制信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。
- [70] 具体地，按键开关单元50优选为按键开关K1，但也可以是其它类型的开关如触摸开关等，并不限于此，在本发明第一优选实施例的电子烟雾化控制方法中，触摸开关单元10包括连接电池杆导电表面的触摸感应开关101以及和触摸感应开关101连接的感应信号处理模块102，其雾化控制方法具体为：
- [71] 当用户接触电池杆时（包括用手触摸或吸烟时口腔接触电子烟导电表面上的触摸感应区域），触摸感应开关101产生感应信号并将该感应信号发送至感应信号处理模块102，感应信号处理模块102将该感应信号进行放大处理，并输出一

控制信号（在本实施例中，该控制信号为低电平信号）；

[72] 按下按键开关K1，该控制信号经按键开关K1传送给控制模块20；

[73] 控制模块20接收该控制信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

[74] 具体地，在本发明第二优选实施例的电子烟控制方法中，触摸开关单元10包括电阻R2~R4、以及开关管Q1，电池的正接线端B+连接电子烟本体的导电表面，电阻R4连接设于电子烟导电表面上的按键开关K1的顶部金属帽，其控制方法具体包括：

[75] 当用户握住电池杆时，导电表面上电连接电池正极的电池电压通过肌肤导电传送给按键开关的顶部金属帽，并经电阻R4传送到开关管Q1的基极，开关管Q1导通，输出控制信号，在本实施例中该控制信号为低电平信号；

[76] 按下按键开关K1，该低电平信号经按键开关K1传送到控制模块20；

[77] 控制模块20接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

[78] 具体地，在本发明第三优选实施例的电子烟控制方法中，触摸开关单元10包括运算放大器U1以及电阻R5，运算放大器U1的反相输入端连接按键开关的顶部金属帽，电池的正接线端连接电池杆的导电表面，其控制方法具体包括：

[79] 当用户手握电池杆时，电池杆导电表面上的电池电压通过肌肤导电经按键开关K1顶部金属帽传送到运算放大器U1的反相输入端，运算放大器U1输出控制信号（在本实施例中，该控制信号也为低电平信号）；

[80] 按下按键开关K1，该低电平信号经按键开关K1传送到控制模块20；

[81] 控制模块20接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

[82] 因此，实施本发明的电子烟及其雾化控制方法，在电子烟本体的导电表面上依次电连接触摸开关单元和按键开关单元，其中，按键开关单元包括按键开关，即根据触摸感应功能或者通过肌肤导电并结合按键开关来实现对电子烟的控制，使得电子烟在运输过程中或生活中乱堆乱放的时候，只要用户不需使用电子烟，也就不会接触电子烟本体的导电表面，即使电子烟因挤压或碰撞造成按

键开关被误触发，电热丝也不会发热，电子烟不工作，也就不存在安全隐患。有效解决了现有的按键开关经常被误触发时电子烟即可工作，从而导致电子烟发热频率高，缩短电子烟的寿命，电全性能低等问题。

- [83] 上面结合附图对本发明的实施例进行了描述，但是本发明并不局限于上述的具体实施方式，上述的具体实施方式仅仅是示意性的，而不是限制性的，本领域的普通技术人员在本发明的启示下，在不脱离本发明宗旨和权利要求所保护的范围情况下，还可做出很多形式，这些均属于本发明的保护之内。

权利要求书

- [权利要求 1] 一种电子烟，包括电子烟本体，所述电子烟本体设置有利于雾化烟油的雾化器（1）以及用于为雾化器提供电源的电池杆（2），其特征在于，所述电子烟本体的外周面上设置有导电表面，该电子烟还包括电连接所述导电表面的触摸开关单元（10）、与所述触摸开关单元（10）串联连接的按键开关单元（50）、以及与所述按键开关单元（50）连接的控制模块（20）；
- 所述触摸开关单元（10）用于在用户接触所述导电表面时输出一控制信号至所述按键开关单元（50）；
- 所述按键开关单元（50）用于在开启时将该控制信号传送给所述控制模块（20）；
- 所述控制模块（20）用于根据接收到的控制信号对所述雾化器（1）进行控制，实现对电子烟的烟油进行雾化。
- [权利要求 2] 根据权利要求1所述的电子烟，其特征在于，所述电子烟的吸烟端包覆有导电纸，所述导电纸的表面为所述导电表面。
- [权利要求 3] 根据权利要求1所述的电子烟，其特征在于，所述按键开关单元（50）包括按键开关（K1）；所述雾化器（1）包括与所述控制模块（20）连接，且用于加热油烟使其发出烟雾的电热丝（30）。
- [权利要求 4] 根据权利要求3所述的电子烟，其特征在于，所述触摸开关单元（10）包括电连接所述导电表面的触摸感应开关（101）以及与所述触摸感应开关（101）连接的感应信号处理模块（102）；
- 所述触摸感应开关（101）用于在用户接触所述导电表面时发送感应信号给所述感应信号处理模块（102）；
- 所述感应信号处理模块（102）用于对接收的所述感应信号进行放大处理并输出控制信号，在所述按键开关（K1）被按下时将该控制信号经所述按键开关（K1）传送给所述控制模块（20）。
- [权利要求 5] 根据权利要求4所述的电子烟，其特征在于，所述触摸感应开关（101）为电连接所述导电表面的感应电容（C）。

- [权利要求 6] 根据权利要求5所述的电子烟，其特征在于，所述感应信号处理模块（102）由TTP224芯片实现。
- [权利要求 7] 根据权利要求6所述的电子烟，其特征在于，所述感应信号处理模块（102）的第“1”引脚与所述感应电容（C）连接，所述感应信号处理模块（102）的第“10”引脚分别连接所述电池（40）的正接线端和第一电阻（R1）的一端，所述电池（40）的负接线端接地，所述感应信号处理模块（102）的第“16”引脚和所述第一电阻（R1）的另一端均与所述按键开关（K1）的一端连接，所述按键开关（K1）的另一端与所述控制模块（20）连接。
- [权利要求 8] 根据权利要求7所述的电子烟，其特征在于，所述控制模块（20）的输入引脚与所述按键开关（K1）连接，所述控制模块（20）的电源引脚分别与所述电池（40）的正接线端和第一电容（C1）的一端连接，所述第一电容（C1）的另一端与电池（40）的负接线端连接，所述控制模块（20）的输出引脚与所述电热丝（30）连接。
- [权利要求 9] 根据权利要求3所述的电子烟，其特征在于，所述触摸开关单元（10）包括第二电阻（R2）以及开关管（Q1），所述电池（40）的正接线端电连接所述导电表面，所述开关管（Q1）的基极电连接设在所述导电表面上的按键开关（K1）的顶部金属帽（J1），所述开关管（Q1）的集电极分别与所述第二电阻（R2）的一端和所述按键开关（K1）的一端连接，所述第二电阻（R2）的另一端与所述电池（40）的正接线端连接，所述开关管（Q1）的发射极接地，所述按键开关（K1）的另一端与所述控制模块（20）连接。
- [权利要求 10] 根据权利要求9所述的电子烟，其特征在于，所述触摸开关单元（10）还包括连接在所述按键开关（K1）的顶部金属帽（J1）和所述开关管（Q1）的基极之间的第四电阻（R4）以及连接在所述电池（40）的正接线端和所述开关管（Q1）的基极之间的第三电阻（R3）。

- [权利要求 11] 根据权利要求3所述的电子烟，其特征在于，所述触摸开关单元（10）包括运算放大器（U1）以及第五电阻（R5），所述运算放大器（U1）的反相输入端电连接设在所述导电表面上的所述按键开关（K1）的顶部金属帽（J1），所述电池（40）的正接线端连接所述导电表面，所述运算放大器（U1）的同相输入端与所述电池（40）的负接线端连接，所述运算放大器（U1）的输出端分别与所述第五电阻（R5）的一端和所述按键开关（K1）的一端连接，所述第五电阻（R5）的另一端与所述电池（40）的正接线端连接，所述按键开关（K1）的另一端与所述控制模块（20）连接。
- [权利要求 12] 一种电子烟雾化控制方法，其特征在于，包括：
电连接至电子烟本体外周面的导电表面的触摸开关单元（10）检测到用户的触摸动作后输出一控制信号；
与所述触摸开关单元（10）电连接的按键开关单元（50）在开启后将所述控制信号传送给所述控制模块（20）；
所述控制模块（20）根据接收到的控制信号控制电子烟的雾化器（1）进行雾化烟油。
- [权利要求 13] 根据权利要求12所述的电子烟雾化控制方法，其特征在于，所述按键开关单元（50）包括按键开关（K1）；所述雾化器（1）包括与所述控制模块（20）连接，且用于加热油烟使其发出烟雾的电热丝（30）。
- [权利要求 14] 根据权利要求13所述的电子烟控制方法，其特征在于，所述触摸开关单元（10）包括电连接所述导电表面的触摸感应开关（101）以及和所述触摸感应开关（101）连接的感应信号处理模块（102），所述控制方法具体包括：
当用户接触所述导电表面并按下所述按键开关（K1）时，所述触摸感应开关（101）产生感应信号并将该感应信号发送至所述感应信号处理模块（102），所述感应信号处理模块（102）将该感应信号进行放大处理，并输出一低电平信号给所述按键开关（K1）

的一端；

此时所述按键开关（K1）已闭合，该低电平信号经按键开关（K1）的另一端传送给所述控制模块（20）；

所述控制模块（20）接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

[权利要求 15]

根据权利要求13所述的电子烟控制方法，其特征在于，所述触摸开关单元（10）包括第二电阻（R2）、第三电阻（R3）、第四电阻（R4）以及开关管（Q1），所述电池（40）的正接线端电连接所述导电表面，所述第四电阻（R4）连接设在所述导电表面上的所述按键开关（K1）的顶部金属帽（J1），所述控制方法具体包括：

当用户握住所述导电表面并按下所述按键开关（K1）时，所述导电表面上的电池电压通过肌肤导电传送给所述按键开关（K1）的顶部金属帽（J1），并经所述第四电阻（R4）传送到所述开关管（Q1）的基极，所述开关管（Q1）导通，输出低电平信号给所述按键开关（K1）的一端；

此时所述按键开关（K1）已闭合，该低电平信号经所述按键开关（K1）的另一端传送到所述控制模块（20）；

所述控制模块（20）接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

[权利要求 16]

根据权利要求13所述的电子烟控制方法，其特征在于，所述触摸开关单元（10）包括运算放大器（U1）以及第五电阻（R5），所述运算放大器（U1）的反相输入端连接设在所述导电表面上的所述按键开关（K1）的顶部金属帽（J1），所述电池（40）的正接线端电连接所述导电表面，所述控制方法具体包括：

当用户握住所述导电表面并按下所述按键开关（K1）时，所述导电表面上的电池电压通过肌肤导电经所述按键开关（K1）的顶部金属帽（J1）传送到所述运算放大器（U1）的反相输入端，所述

运算放大器（U1）输出低电平信号给所述按键开关（K1）的一端；

此时按键开关（K1）已闭合，该低电平信号经所述按键开关（K1）的另一端传送到所述控制模块（20）；

所述控制模块（20）接收该低电平信号后，对雾化器进行控制，实现对电子烟的烟油进行雾化。

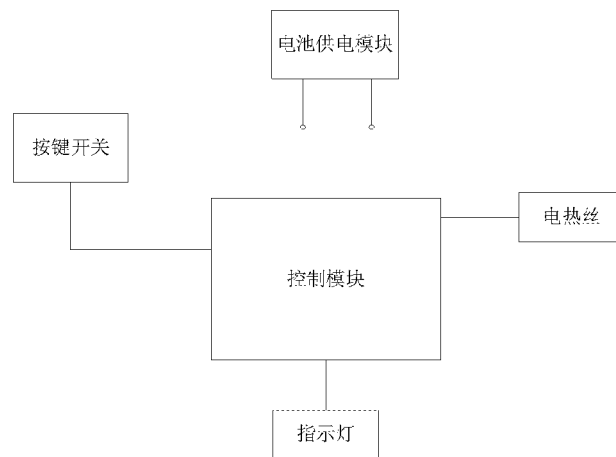


图 1



图 2

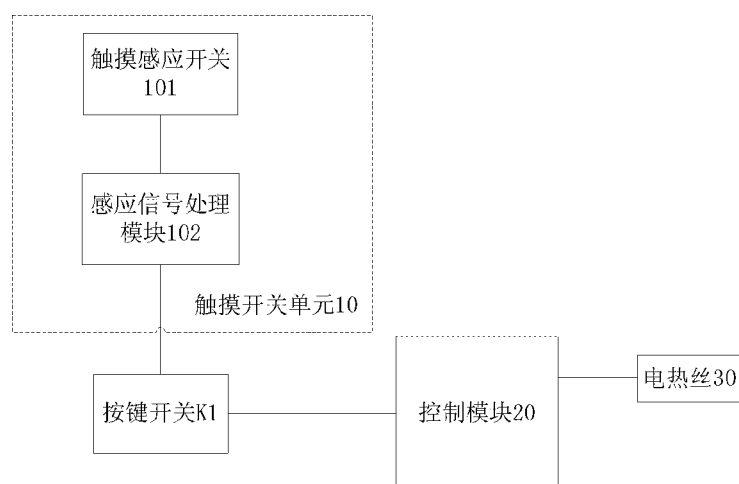


图 3

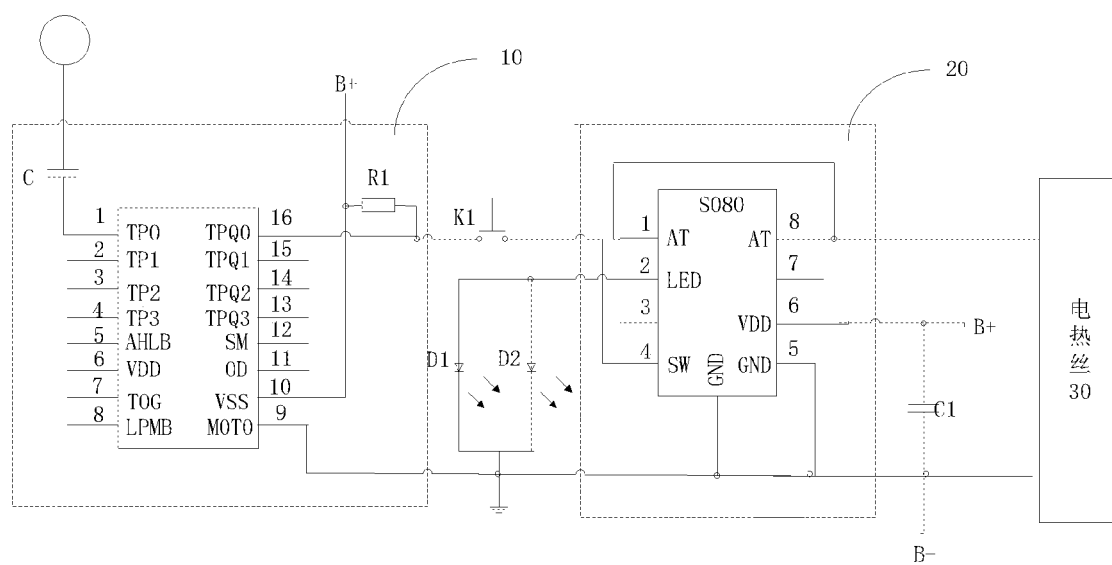


图 4

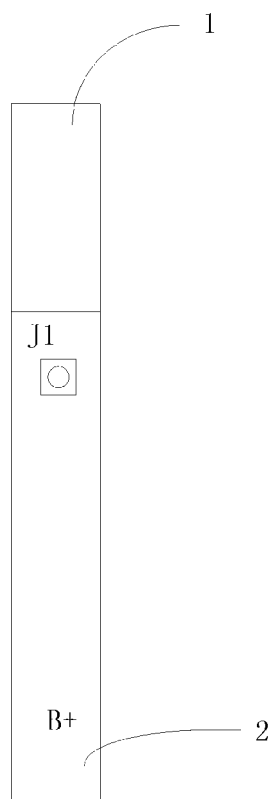


图 5

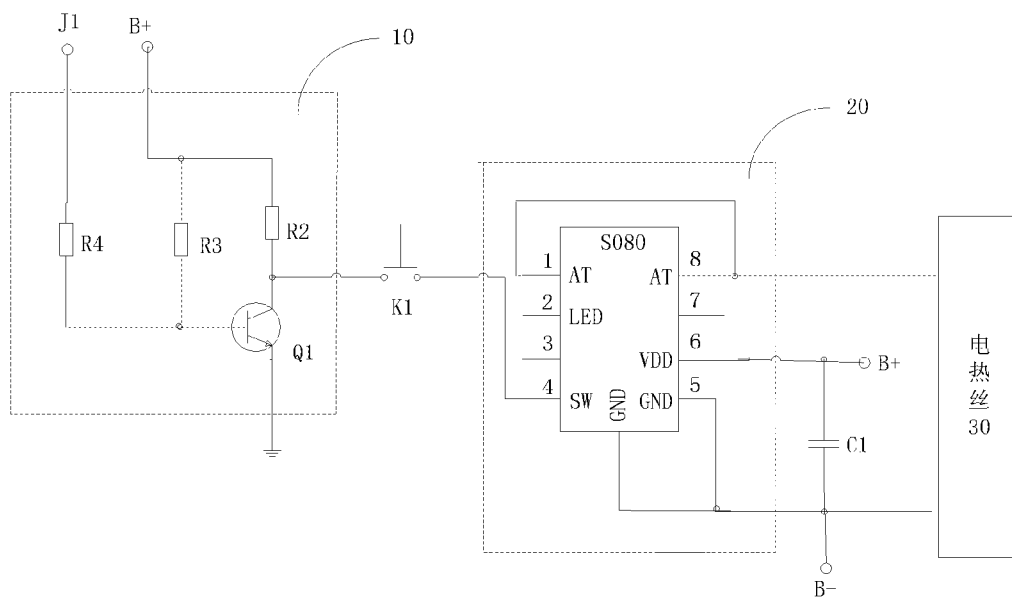


图 6

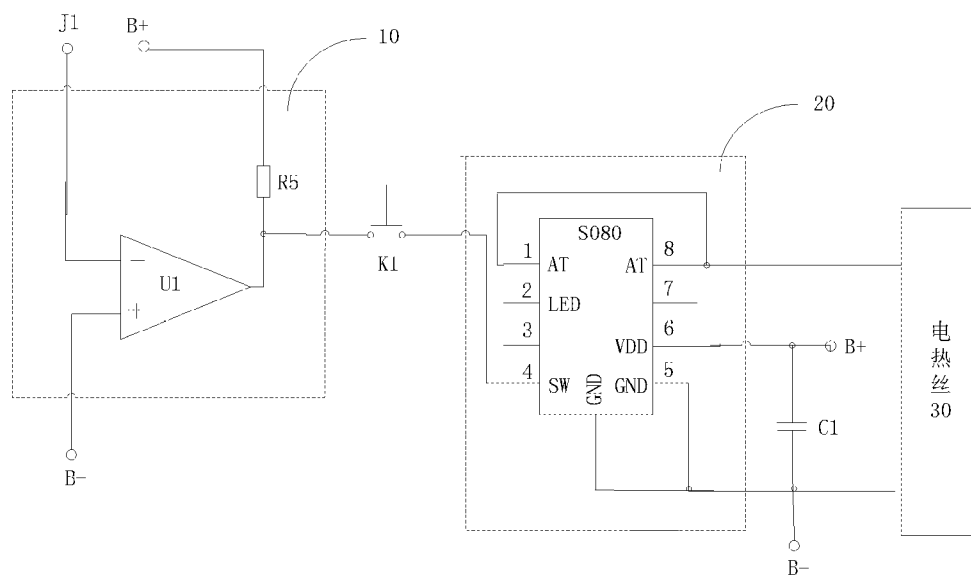


图 7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2014/076715

A. CLASSIFICATION OF SUBJECT MATTER

A24F 47/00 (2006.01) i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A24F 47; A61M 11; A61M 15

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CNXTXT; CNABS; VEN: dual, electr+, atomize, imitate, simulate, substitute, cigar+, tobacco, mult+, plural, two, switch, on-off

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 203378562 U (LIU, Qiuming), 08 January 2014 (08.01.2014), description, pages 2-4, and figures 1-6	1-16
Y	CN 102396783 A (CHEN, Aiguang), 04 April 2012 (04.04.2012), description, pages 3 and 4, and figures 1-3	1-16
Y	CN 203314106 U (LIU, Qiuming), 04 December 2013 (04.12.2013), description, pages 2 and 3, and figure 1	1-16
Y	CN 202800121 U (LONG, Gongyun), 20 March 2013 (20.03.2013), description, pages 2 and 3, and figures 1 and 2	1-16
Y	WO 2013147492 A1 (ENBRIGHT CO., LTD.), 03 October 2013 (03.10.2013), abstract	1-16
A	US 2014069444 A1 (CYPHERT, G. et al.), 13 March 2014 (13.03.2014), the whole document	1-16
A	CN 102940314 A (JOYTECH (CHANGZHOU) ELECTRONICS CO., LTD.), 27 February 2013 (27.02.2013), the whole document	1-16

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search 30 January 2015 (30.01.2015)	Date of mailing of the international search report 17 February 2015 (17.02.2015)
Name and mailing address of the ISA/CN: State Intellectual Property Office of the P. R. China No. 6, Xitucheng Road, Jimenqiao Haidian District, Beijing 100088, China Facsimile No.: (86-10) 62019451	Authorized officer ZHANG, Yucui Telephone No.: (86-10) 62084123

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2014/076715**C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CN 103181622 A (CHINA TOBACCO HUBEI INDUSTRIAL CO., LTD. et al.), 03 July 2013 (03.07.2013), the whole document	1-16

Form PCT/ISA/210 (continuation of second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2014/076715

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
CN 203378562 U	08 January 2014	None	
CN 102396783 A	04 April 2012	CN 102396783 B	02 October 2013
CN 203314106 U	04 December 2013	None	
CN 202800121 U	20 March 2013	None	
WO 2013147492 A1	03 October 2013	US 2014334804 A1	13 November 2014
		CN 104114049 A	22 October 2014
US 2014069444 A1	13 March 2014	None	
CN 102940314 A	27 February 2013	None	
CN 103181622 A	03 July 2013	None	

Form PCT/ISA/210 (patent family annex) (July 2009)

<p>A. 主题的分类</p> <p>A24F 47/00(2006.01)i</p> <p>按照国际专利分类(IPC)或者同时按照国家分类和IPC两种分类</p>																										
<p>B. 检索领域</p> <p>检索的最低限度文献(标明分类系统和分类号)</p> <p>A24F47; A61M11; A61M15</p> <p>包含在检索领域中的除最低限度文献以外的检索文献</p> <p>在国际检索时查阅的电子数据库(数据库的名称, 和使用的检索词(如使用))</p> <p>CNXT;CNABS;VEN:电子, 雾化, 仿真, 模拟, 替代, 烟, 多, 二, 两, 双, 开关, electr+, atomize, imitate, simulate, substitute, cigar+, tobacco,mult+, plural, two, switch, on-off</p>																										
<p>C. 相关文件</p> <table border="1"> <thead> <tr> <th>类 型*</th> <th>引用文件, 必要时, 指明相关段落</th> <th>相关的权利要求</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>CN 203378562 U (刘秋明) 2014年 1月 08日 (2014 - 01 - 08) 说明书第2-4页, 附图1-6</td> <td>1-16</td> </tr> <tr> <td>Y</td> <td>CN 102396783 A (陈爱光) 2012年 4月 04日 (2012 - 04 - 04) 说明书第3、4页, 附图1-3</td> <td>1-16</td> </tr> <tr> <td>Y</td> <td>CN 203314106 U (刘秋明) 2013年 12月 04日 (2013 - 12 - 04) 说明书第2、3页, 附图1</td> <td>1-16</td> </tr> <tr> <td>Y</td> <td>CN 202800121 U (龙功运) 2013年 3月 20日 (2013 - 03 - 20) 说明书第2、3页, 附图1、2</td> <td>1-16</td> </tr> <tr> <td>Y</td> <td>WO 2013147492 A1 (ENBRIGHT CO LTD) 2013年 10月 03日 (2013 - 10 - 03) 摘要</td> <td>1-16</td> </tr> <tr> <td>A</td> <td>US 2014069444 A1 (CYPHERT GILBERT等) 2014年 3月 13日 (2014 - 03 - 13) 全文</td> <td>1-16</td> </tr> <tr> <td>A</td> <td>CN 102940314 A (卓尔悦常州电子科技有限公司) 2013年 2月 27日 (2013 - 02 - 27) 全文</td> <td>1-16</td> </tr> </tbody> </table>			类 型*	引用文件, 必要时, 指明相关段落	相关的权利要求	X	CN 203378562 U (刘秋明) 2014年 1月 08日 (2014 - 01 - 08) 说明书第2-4页, 附图1-6	1-16	Y	CN 102396783 A (陈爱光) 2012年 4月 04日 (2012 - 04 - 04) 说明书第3、4页, 附图1-3	1-16	Y	CN 203314106 U (刘秋明) 2013年 12月 04日 (2013 - 12 - 04) 说明书第2、3页, 附图1	1-16	Y	CN 202800121 U (龙功运) 2013年 3月 20日 (2013 - 03 - 20) 说明书第2、3页, 附图1、2	1-16	Y	WO 2013147492 A1 (ENBRIGHT CO LTD) 2013年 10月 03日 (2013 - 10 - 03) 摘要	1-16	A	US 2014069444 A1 (CYPHERT GILBERT等) 2014年 3月 13日 (2014 - 03 - 13) 全文	1-16	A	CN 102940314 A (卓尔悦常州电子科技有限公司) 2013年 2月 27日 (2013 - 02 - 27) 全文	1-16
类 型*	引用文件, 必要时, 指明相关段落	相关的权利要求																								
X	CN 203378562 U (刘秋明) 2014年 1月 08日 (2014 - 01 - 08) 说明书第2-4页, 附图1-6	1-16																								
Y	CN 102396783 A (陈爱光) 2012年 4月 04日 (2012 - 04 - 04) 说明书第3、4页, 附图1-3	1-16																								
Y	CN 203314106 U (刘秋明) 2013年 12月 04日 (2013 - 12 - 04) 说明书第2、3页, 附图1	1-16																								
Y	CN 202800121 U (龙功运) 2013年 3月 20日 (2013 - 03 - 20) 说明书第2、3页, 附图1、2	1-16																								
Y	WO 2013147492 A1 (ENBRIGHT CO LTD) 2013年 10月 03日 (2013 - 10 - 03) 摘要	1-16																								
A	US 2014069444 A1 (CYPHERT GILBERT等) 2014年 3月 13日 (2014 - 03 - 13) 全文	1-16																								
A	CN 102940314 A (卓尔悦常州电子科技有限公司) 2013年 2月 27日 (2013 - 02 - 27) 全文	1-16																								
<p>☒ 其余文件在C栏的续页中列出。 ☒ 见同族专利附件。</p>																										
<p>* 引用文件的具体类型:</p> <p>“A” 认为不特别相关的表示了现有技术一般状态的文件</p> <p>“E” 在国际申请日的当天或之后公布的在先申请或专利</p> <p>“L” 可能对优先权要求构成怀疑的文件, 或为确定另一篇引用文件的公布日而引用的或者因其他特殊理由而引用的文件(如具体说明的)</p> <p>“O” 涉及口头公开、使用、展览或其他方式公开的文件</p> <p>“P” 公布日先于国际申请日但迟于所要求的优先权日的文件</p> <p>“T” 在申请日或优先权日之后公布, 与申请不相抵触, 但为了解发明之理论或原理的在后文件</p> <p>“X” 特别相关的文件, 单独考虑该文件, 认定要求保护的发明不是新颖的或不具有创造性</p> <p>“Y” 特别相关的文件, 当该文件与另一篇或者多篇该类文件结合并且这种结合对于本领域技术人员为显而易见时, 要求保护的发明不具有创造性</p> <p>“&” 同族专利的文件</p>																										
<p>国际检索实际完成的日期</p> <p>2015年 1月 30日</p>		<p>国际检索报告邮寄日期</p> <p>2015年 2月 17日</p>																								
<p>ISA/CN的名称和邮寄地址:</p> <p>中华人民共和国国家知识产权局(ISA/CN)</p> <p>北京市海淀区蓟门桥西土城路6号</p> <p>100088 中国</p> <p>传真号 (86-10)62019451</p>		<p>授权官员</p> <p>张羽霖</p> <p>电话号码 (86-10)62084123</p>																								

表 PCT/ISA/210 (第2页) (2009年7月)

类 型*	引用文件，必要时，指明相关段落	相关的权利要求
A	CN 103181622 A (湖北中烟工业有限责任公司等) 2013年 7月 03日 (2013 - 07 - 03) 全文	1-16

2529

国际检索报告
关于同族专利的信息

国际申请号

PCT/CN2014/076715

检索报告引用的专利文件			公布日 (年/月/日)	同族专利	公布日 (年/月/日)
CN	203378562	U	2014年 1月 08日	无	
CN	102396783	A	2012年 4月 04日	CN 102396783	B 2013年 10月 02日
CN	203314106	U	2013年 12月 04日	无	
CN	202800121	U	2013年 3月 20日	无	
WO	2013147492	A1	2013年 10月 03日	US 2014334804	A1 2014年 11月 13日
				CN 104114049	A 2014年 10月 22日
US	2014069444	A1	2014年 3月 13日	无	
CN	102940314	A	2013年 2月 27日	无	
CN	103181622	A	2013年 7月 03日	无	

表 PCT/ISA/210 (同族专利附件) (2009年7月)

Bibliographic data: WO2015168828 (A1) — 2015-11-12

ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREFOR

Page bookmark WO2015168828 (A1) - ELECTRONIC CIGARETTE AND ATOMIZATION CONTROL METHOD THEREFOR

Inventor(s): LIU QIUMING [CN] ± (LIU, QIUMING)

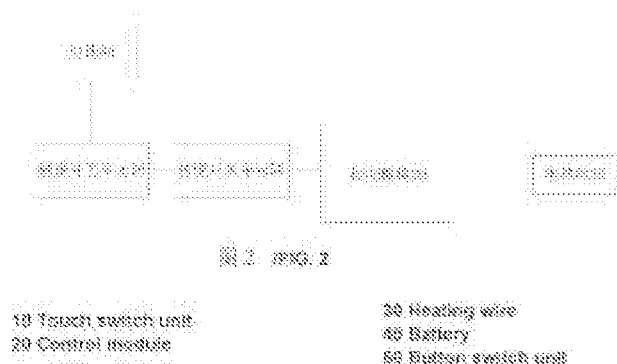
Applicant(s): KIMREE HI TECH INC ± (KIMREE HI-TECH INC)

Classification: - international: A24F47/00
- cooperative: A24F47/00

Application number: WO2014CN76715 20140504

Priority number(s): WO2014CN76715 20140504

Abstract of WO2015168828 (A1)



An electronic cigarette and an atomization control method therefor. The electronic cigarette comprises an electronic cigarette body. The electronic cigarette body is provided with an atomizer (1) and a battery rod (2). A conductive surface is provided on an outer circumferential face of the electronic cigarette body. The electronic cigarette also comprises a touch switch unit (10) which is electronically connected to the conductive surface, a button switch unit (50) which is connected to the touch switch unit (10) in series, and a control module (20) which is connected to the button switch unit (50); the touch switch unit (10) is used to output a control signal to the button switch unit (50) when a user touches the conductive surface; the button switch unit (50) is used to transmit the control signal to the control module (20) when being started; and the control

module (20) is used to control the atomizer (1) according to the received control signal, so as to realize the atomization of the tobacco tar of the electronic cigarette. Beneficial effects: the electronic cigarette is controlled by way of combining the touch switch unit and the button switch unit, so that a heating wire does not generate heat even if the button switch is mis-triggered due to the electronic cigarette being squeezed or knocked, and the security performance is high.

Electronic Patent Application Fee Transmittal				
Application Number:		14925968		
Filing Date:		28-Oct-2015		
Title of Invention:		NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		
First Named Inventor/Applicant Name:		Adam BOWEN		
Filer:		Richard Douglas Shoop/Brian Flick		
Attorney Docket Number:		13211-713.303		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
Submission- Information Disclosure Stmt	1806	1	180	180
Total in USD (\$)				180

Electronic Acknowledgement Receipt

EFS ID:	26322723
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	12-JUL-2016
Filing Date:	28-OCT-2015
Time Stamp:	12:51:13
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$ 180
RAM confirmation Number	071216INTEFSW00011347504050
Deposit Account	504050
Authorized User	Richard Shoop

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_7-12-2016.pdf	368505	yes	5
			49db8cab8b70ba2fa94a2301c7196a74079d99e1		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Transmittal Letter		1	3	
	Information Disclosure Statement (IDS) Form (SB08)		4	5	
Warnings:					
Information:					
2	Foreign Reference	WO2015149647A1wEngAbs.pdf	4126062	no	30
			5befb950204f07116668f0505bde16b475a60b4c		
Warnings:					
Information:					
3	Foreign Reference	WO2015168828A1wEngAbs.pdf	3569086	no	30
			5ee87f51ce7ac3a070eabc7220a3d17100792211		
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30801	no	2
			64f4946aa153fa64a44ecd4b4490c28cf440066b		
Warnings:					
Information:					
Total Files Size (in bytes):			8094454		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on 7-12-2016.

Adam Bowen
Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
 First Named Inventor : Adam Bowen
 Filed : October 28, 2015
 Art Unit : 1747
 Examiner : Mayes, Dionne Walls
 Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
 AND METHODS THEREOF
 Customer No. : 66854

INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and /or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT

**37 CFR §1.97(b)**

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ 1). Within 3 months of the application filing date, or
☐ 2). Within 3 months of entry of a national stage as set forth in § 1.491, or
☐ 3). Before the mail date of a first Office Action on the merits, or
☐ 3a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
☐ 4). Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
☐ 4a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☐ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☐ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☐ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☐ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☒ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under § 1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement

--AND--

B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☒ **37 CFR §1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☒ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☐ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☐ **37 CFR §1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☐ 3). A copy of each application specification is not submitted because the application is stored in the IFW. Cite no(s):

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☐ **37 CFR §1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☐ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

- ☐ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**
- ☐ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☒ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**
- ☒ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☒ **2a).** An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): 639 and 640 **--AND/OR--**
- ☐ **2b).** A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): **--OR--**
- ☐ **3).** A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

STATEMENT UNDER 37 CFR § 1.97(e)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement.
- ☒ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

STATEMENT UNDER 37 CFR § 1.704(d)

- ☐ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

- ☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$180.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

Dated: 7/12/16

By: 
Richard D. Shoop, Reg. No. 45,763

Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P. O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/925,968	10/28/2015	Adam BOWEN	13211-713.303	2707
66854	7590	07/28/2016		
SHAY GLENN LLP 2755 CAMPUS DRIVE SUITE 210 SAN MATEO, CA 94403			EXAMINER MAYES, DIONNE WALLS	
			ART UNIT	PAPER NUMBER
			1747	
			NOTIFICATION DATE	DELIVERY MODE
			07/28/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@shayglenn.com

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	14/925,968	BOWEN ET AL.	
	Examiner	Art Unit	
	DIONNE W. MAYES	1747	

All participants (applicant, applicant's representative, PTO personnel):

(1) DIONNE W. MAYES. (3) _____.

(2) RICHARD SHOOP. (4) _____.

Date of Interview: 12 July 2016.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: Those of Record.

Identification of prior art discussed: Collett et al (US. Pat. No. 8,881,737), Gonda (US. Pat. App. Pub. 2014/0261474) and Bowen '717 (US. Pat. App. Pub. 2009/0151717).

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Examiner Mayes contacted Applicant's representative, Mr. Shoop, pursuant to the Request, filed on 6/15/2016, under the AFCP 2.0 Program. In the Request, Applicant proposed amending the independent claims, in a substantial manner, so as to require further search/consideration. After review of the proposed amendments, and a quick prior art search, Examiner Mayes determined that a new prior art reference, such as Collett et al, could be used (in lieu of existing primary reference Griffith, Jr. et al) to address the proposed new recitation regarding "wick/wicking". Examiner Mayes then submitted that the existing references to Gonda and Bowen '717 were still proper to reject the proposed new claim recitation regarding "Cmax". As such, Examiner Mayes indicated that the proposed claim amendments would not be entered, as they do not appear to render the claimed invention definable over the prior art, but that she'd be happy to further consider the claimed invention, officially, - as well as the Declaration filed under 37 CFR 1.132 - upon the filing of a Continued application, i.e. an RCE. Mr. Shoop stood firm on Applicant's position that the proposed claims defined over the prior art of record, but indicated that he would take what was discussed into consideration and file an official response to the Final Rejection accordingly.

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/DIONNE W MAYES/ Examiner, Art Unit 1747	
---	--

Advisory Action Before the Filing of an Appeal Brief	Application No. 14/925,968	Applicant(s) BOWEN ET AL.	
	Examiner DIONNE W. MAYES	Art Unit 1747	AIA (First Inventor to File) Status Yes

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 June 2016 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☐ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance;
 (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires _____ months from the mailing date of the prior Advisory Action or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.

Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANT'S FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because

a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);

b) ☐ They raise the issue of new matter (see NOTE below);

c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): (a) ☒ will not be entered, or (b) ☐ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

9. ☒ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

10. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

11. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

12. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

13. ☐ Note the attached Information *Disclosure Statement(s)*. (PTO/SB/08) Paper No(s). _____

14. ☒ Other: See attached PTO-2323 and PTO-413B forms.

STATUS OF CLAIMS

15. The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1-4,6-10,12-18 and 20.

Claim(s) withdrawn from consideration: _____.

/MICHAEL H WILSON/ Supervisory Patent Examiner, Art Unit 1747	/DIONNE W MAYES/ Examiner, Art Unit 1747
--	---

Continuation of 3. NOTE: Applicant has proposed substantially amending the independent claims in a manner that significantly changes the scope of said claims. Specifically, it proposes the addition, in independent claims 1 and 13 of "a Cmax of over 10 ng/mL on average" and, also, in independent claims 1, 7 and 13 of "wick/wicking" recitation. Such amendment would raise new issues that would require further consideration and/or search, and would most likely require the application of new prior art references to reject the claims. As such, the proposed amendment has not been entered.

Examiner-Initiated Interview Summary	Application No. 14/925,968	Applicant(s) BOWEN ET AL.	
	Examiner DIONNE W. MAYES	Art Unit 1747	

All participants (applicant, applicant's representative, PTO personnel):

(1) DIONNE W. MAYES. (3) _____.

(2) RICHARD SHOOP. (4) _____.

Date of Interview: 12 July 2016.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: Those of Record.

Identification of prior art discussed: Collett et al (US. Pat. No. 8,881,737), Gonda (US. Pat. App. Pub. 2014/0261474) and Bowen '717 (US. Pat. App. Pub. 2009/0151717).

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Examiner Mayes contacted Applicant's representative, Mr. Shoop, pursuant to the Request, filed on 6/15/2016, under the AFCP 2.0 Program. In the Request, Applicant proposed amending the independent claims, in a substantial manner, so as to require further search/consideration. After review of the proposed amendments, and a quick prior art search, Examiner Mayes determined that a new prior art reference, such as Collett et al, could be used (in lieu of existing primary reference Griffith, Jr. et al) to address the proposed new recitation regarding "wick/wicking". Examiner Mayes then submitted that the existing references to Gonda and Bowen '717 were still proper to reject the proposed new claim recitation regarding "Cmax". As such, Examiner Mayes indicated that the proposed claim amendments would not be entered, as they do not appear to render the claimed invention definable over the prior art, but that she'd be happy to further consider the claimed invention, officially, - as well as the Declaration filed under 37 CFR 1.132 - upon the filing of a Continued application, i.e. an RCE. Mr. Shoop stood firm on Applicant's position that the proposed claims defined over the prior art of record, but indicated that he would take what was discussed into consideration and file an official response to the Final Rejection accordingly.

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/DIONNE W MAYES/ Examiner, Art Unit 1747	
---	--

<p style="text-align: center;">AFCP 2.0 Decision</p>	<p>Application No.</p> <p>14/925,968</p>	<p>Applicant(s)</p> <p>BOWEN ET AL.</p>
	<p>Examiner</p> <p>DIONNE W. MAYES</p>	<p>Art Unit</p> <p>1747</p>

This is in response to the After Final Consideration Pilot request filed 15 June 2016.

1. **Improper Request** – The AFCP 2.0 request is improper for the following reason(s) and the after final amendment submitted with the request will be treated under pre-pilot procedure.

- ☐ An AFCP 2.0 request form PTO/SB/434 (or equivalent document) was not submitted.
- ☐ A non-broadening amendment to at least one independent claim was not submitted.
- ☐ A proper AFCP 2.0 request was submitted in response to the most recent final rejection.
- ☐ Other:

2. **Proper Request**

- A. After final amendment submitted with the request will not be treated under AFCP 2.0.

The after final amendment cannot be reviewed and a search conducted within the guidelines of the pilot program.

- ☐ The after final amendment will be treated under pre-pilot procedure.

- B. Updated search and/or completed additional consideration.

The examiner performed an updated search and/or completed additional consideration of the after final amendment within the time authorized for the pilot program. The result(s) of the updated search and/or completed additional consideration are:

- ☐ 1. All of the rejections in the most recent final Office action are overcome and a Notice of Allowance is issued herewith.
- ☒ 2. The after final amendment would not overcome all of the rejections in the most recent final Office action. See attached interview summary for further details.
- ☐ 3. The after final amendment was reviewed, and it raises a new issue(s). See attached interview summary for further details.
- ☐ 4. The after final amendment raises new issues, but would overcome all of the rejections in the most recent final Office action. A decision on determining allowability could not be made within the guidelines of the pilot. See attached interview summary for further details, including any newly discovered prior art.
- ☐ 5. Other:

Examiner Note: Please attach an interview summary when necessary as described above.

Response dated: June 15, 2016

App. No.: 14/925,968; Filed: October 28, 2015

Response to Office Action of May 13, 2016

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick, wherein:
 - a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and
 - c. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from the fluid storage compartment to the heating element and heating at least a portion of the nicotine formulation to generate an inhalable aerosol between about 100°C and about 300°C;wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL on average, and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
2. (Currently amended) The method of claim 1, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between about 1:1 and 1:3.
3. (Original) The method of claim 1, wherein the nicotine formulation further comprises at least one flavorant.
4. (Original) The method of claim 1, wherein the nicotine concentration is about 4.5%.
5. (Cancelled)

6. (Original) The method of claim 1, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
7. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier within a fluid storage compartment connected to a heating element by a wick, wherein:
- a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the nicotine formulation comprises protonated nicotine;
 - c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol;
 - d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the low-temperature vaporizer; and
 - e. operation of the low-temperature vaporizer comprises wicking the nicotine formulation from the fluid storage compartment to the heating element and heating at least a portion of the nicotine formulation between about 100°C and 300°C to generate an inhalable aerosol;
- wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
8. (Currently amended) The method of claim 7, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
9. (Original) The method of claim 7, wherein the nicotine formulation further comprises at least one flavorant.
10. (Original) The method of claim 7, wherein the nicotine concentration is about 4.5%.

11. (Cancelled)
12. (Original) The method of claim 7, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
13. (Currently amended) A low-temperature vaporizer, comprising:
 - a liquid reservoir;
 - a nicotine formulation within the liquid reservoir, the nicotine formulation comprising:
 - nicotine lactate;
 - propylene glycol; and
 - 90%-30% vegetable glycerol;
 - wherein a concentration of nicotine in the nicotine formulation is from about 0.5% (w/w) to about 20% (w/w);
 - a vaporizing component configured to produce an aerosol from the nicotine formulation by heating at least a portion of the nicotine formulation between 100°C and 300°C,
wherein the liquid reservoir is connected to the vaporizing component by a wick; and
 - a mouthpiece configured to connect to the reservoir for inhalation of the aerosol;
 - wherein inhalation of the aerosol into the user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 min to about 8 min and a Cmax of over 10 ng/mL on average, and further
wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
14. (Original) The electronic cigarette of claim 13, further comprises a battery configured to provide power to the vaporizing component.
15. (Currently amended) The electronic cigarette of claim 13, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
16. (Original) The electronic cigarette of claim 13, wherein the nicotine formulation further comprises at least one flavorant.

Response dated: June 15, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

17. (Original) The electronic cigarette of claim 13, wherein the vaporizing component comprises a heating element in fluid communication with the nicotine formulation.
18. (Original) The electronic cigarette of claim 13, wherein the nicotine concentration is about 4.5%.
19. (Cancelled)
20. (Original) The electronic cigarette of claim 13, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY.DOCKET NO./TITLE	REQUEST ID
14/925,968	10/28/2015	PAX Labs, Inc.	13211-713.303	23382

Acknowledgement of Change to Small Entity Status

The entity status change request below filed through Private PAIR on 08/17/2016 has been accepted.

CERTIFICATIONS:

Change of Entity Status:

✕ Applicant asserting small entity status. See 37 CFR 1.27.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

This portion must be completed by the signatory or signatories making the entity status change in accordance with 37 CFR 1.4(d)(4).

Signature:	/Richard D. Shoop/
Name:	Richard D. Shoop
Registration Number:	45763

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

**Request
for
Continued Examination (RCE)
Transmittal**Address to:
Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam BOWEN
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.

Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, to any international application that does not comply with the requirements of 35 U.S.C. 371, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO on page 2.)

1. **Submission required under 37 CFR 1.114** Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

- a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

i. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____

ii. ☐ Other _____

- b. ☒ Enclosed

i. ☒ Amendment/Reply

iii. ☒ Information Disclosure Statement (IDS)

ii. ☒ Affidavit(s)/ Declaration(s)

iv. ☒ Other Pet. Ext. of Time, Track 1 Request

2. **Miscellaneous**

- a. ☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

b. ☐ Other _____

3. **Fees**

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to

- a. ☒ Deposit Account No. 50-4050

i. ☒ RCE fee required under 37 CFR 1.17(e)

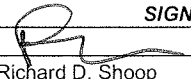
ii. ☒ Extension of time fee (37 CFR 1.136 and 1.17)

iii. ☒ Other Track 1 Request (\$2,000) and Processing Fee (\$70)

- b. ☐ Check in the amount of \$ _____ enclosed

- c. ☐ Payment by credit card (Form PTO-2038 enclosed)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED**

Signature		Date	August 19, 2016
Name (Print/Type)	Richard D. Shoop	Registration No.	45,763

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.

Signature	/Mary Buggie/	Date	August 19, 2016
Name (Print/Type)	Mary Buggie via EFS		

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

**CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION
UNDER 37 CFR 1.102(e) (Page 1 of 1)**

First Named Inventor:	Adam BOWEN	Nonprovisional Application Number (if known):	14/925,968
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

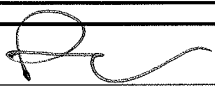
1. The processing fee set forth in 37 CFR 1.17(i)(1), the prioritized examination fee set forth in 37 CFR 1.17(c), and if not already paid, the publication fee set forth in 37 CFR 1.18(d) have been filed with the request. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.
2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims.
3. The applicable box is checked below:

I. ☐ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)

- i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.
---OR---
(b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.
- ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, or the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.

II. ☒ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)

- i. A request for continued examination has been filed with, or prior to, this form.
- ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
- iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
- iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
- v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature 	Date August 19, 2016
Name (Print/Typed) Richard D. Shoop	Practitioner Registration Number 45,763
Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*	
☐ *Total of _____ forms are submitted.	

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)		Docket Number (Optional) 13211-713.303
Application Number 14/925,968	Filed October 28, 2015	
For NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		
Art Unit 1747	Examiner Mayes, Dionne Walls	

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☒ One month (37 CFR 1.17(a)(1))	\$200	\$100	\$50	\$ <u>100</u>
☐ Two months (37 CFR 1.17(a)(2))	\$600	\$300	\$150	\$ _____
☐ Three months (37 CFR 1.17(a)(3))	\$1,400	\$700	\$350	\$ _____
☐ Four months (37 CFR 1.17(a)(4))	\$2,200	\$1,100	\$550	\$ _____
☐ Five months (37 CFR 1.17(a)(5))	\$3,000	\$1,500	\$750	\$ _____

☒ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to
Deposit Account Number 50-4050.

☒ Payment made via EFS-Web.

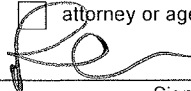
WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 45,763

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____



Signature

August 19, 2016
Date

Richard D. Shoop
Typed or printed name

(650) 212-1700
Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public, which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8
I hereby certify that this correspondence is being transmitted to the
USPTO via EFS-Web on August 19, 2016.

/Mary Buggie/ 8/19/2016
Mary Buggie Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
First Named Inventor: : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL
DEVICES AND METHODS THEREOF
Customer No. : 66854

AMENDMENT AND RESPONSE UNDER 37 C.F.R. § 1.114

This communication is in response to the Advisory Action of July 28, 2016, which in turn responded to the Response to the final Office Action of May 13, 2016 mailed on June 15, 2016. A response to the final Office action was due August 13, 2016. A one-month Petition for Extension of Time is filed herewith, extending the due date up to and including September 13, 2016. Therefore, this response is timely filed.

Applicants submit herewith a Request for Continued Examination (RCE) and the fees for Prioritized Examination - Track 1 status. Finally, a Declaration Under 37 C.F.R. § 1.132 providing support and evidence of commercial success is also submitted herewith.

The Commissioner is authorized to charge any fees to make this filing timely to Deposit Account No. 50-4050.

Amendments to the Claims are shown in the listing of claims that begins on page 2.

Remarks/Arguments begin on page 6 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier in conditions sufficient to form nicotine lactate salt, wherein:
 - a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol; and
 - c. operation of the low-temperature vaporizer comprises wicking the nicotine formulation to a heating element and heating at least a portion of the nicotine formulation to generate an inhalable aerosol of nicotine lactate between about 100°C and about 300°C;wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL on average, and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
2. (Currently amended) The method of claim 1, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between about 1:1 and 1:3.
3. (Original) The method of claim 1, wherein the nicotine formulation further comprises at least one flavorant.
4. (Original) The method of claim 1, wherein the nicotine concentration is about 4.5%.
5. (Cancelled)

6. (Original) The method of claim 1, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
7. (Currently amended) A method of delivering nicotine to a user comprising:
deploying a low-temperature vaporizer comprising a nicotine formulation that comprises nicotine, lactic acid, and a biologically acceptable liquid carrier in conditions sufficient to form nicotine lactate salt, wherein:
 - a. the nicotine concentration is from about 0.5% (w/w) to about 20% (w/w);
 - b. the nicotine formulation comprises protonated nicotine;
 - c. the biologically acceptable liquid carrier comprises propylene glycol and 90%-30% vegetable glycerol;
 - d. the lactic acid does not decompose at room temperature and does not decompose at the operating temperature of the low-temperature vaporizer; and
 - e. operation of the low-temperature vaporizer comprises wicking the nicotine formulation to the heating element and heating at least a portion of the nicotine formulation between about 100°C and 300°C to generate an inhalable aerosol;wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and further wherein the user may modify the amount of nicotine delivered by adjusting inhalation strength.
8. (Currently amended) The method of claim 7, wherein a molar ratio of nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
9. (Original) The method of claim 7, wherein the nicotine formulation further comprises at least one flavorant.
10. (Original) The method of claim 7, wherein the nicotine concentration is about 4.5%.

11. (Cancelled)
12. (Original) The method of claim 7, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
13. (Currently amended) A low-temperature vaporizer, comprising:
a liquid reservoir;
a nicotine formulation within the liquid reservoir, the nicotine formulation comprising:
nicotine lactate;
propylene glycol; and
90%-30% vegetable glycerol;
wherein a concentration of nicotine in the nicotine formulation is from about 0.5% (w/w)
to about 20% (w/w);
a vaporizing component configured to produce an aerosol from the nicotine formulation
by heating at least a portion of the nicotine formulation between 100°C and 300°C,
wherein the liquid reservoir is connected to the vaporizing component by a wick; and
a mouthpiece configured to connect to the reservoir for inhalation of the aerosol;
wherein inhalation of the aerosol into the user's lungs over a period of about 5 minutes at
a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from
about 3 min to about 8 min and a Cmax of over 10 ng/mL on average, and further
wherein the user may modify the amount of nicotine delivered by adjusting inhalation
strength.
14. (Original) The electronic cigarette of claim 13, further comprises a battery configured
to provide power to the vaporizing component.
15. (Currently amended) The electronic cigarette of claim 13, wherein a molar ratio of
nicotine to ~~organic~~ lactic acid is between 1:1 and 1:3.
16. (Original) The electronic cigarette of claim 13, wherein the nicotine formulation
further comprises at least one flavorant.

Response dated: August 19, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

17. (Original) The electronic cigarette of claim 13, wherein the vaporizing component comprises a heating element in fluid communication with the nicotine formulation.
18. (Original) The electronic cigarette of claim 13, wherein the nicotine concentration is about 4.5%.
19. (Cancelled)
20. (Original) The electronic cigarette of claim 13, wherein the inhalable aerosol has a particle size from about 0.1 microns to about 5 microns.
21. (New) The method of claim 1, wherein the nicotine formulation comprises 20% to 50% of propylene glycol and 80% to 50% of vegetable glycerin.
22. (New) The method of claim 7, wherein the nicotine formulation comprises 20% to 50% of propylene glycol and 80% to 50% of vegetable glycerin.

REMARKS

Claims 1-4, 6-10, 12-18 and 20 were pending in this application. By this response, claims 1, 2, 7, 8, 13 and 15 have been amended. New claims 21-22 have been added, and no claims have been cancelled. The amendments to the claims and the new claims are supported throughout the specification, and particularly:

- (a) Support for the amendments to claims 1 and 7 reciting: “...in conditions sufficient to form nicotine lactate salt” may be found at least in paragraphs [0131] and in provisional patent application 61/820,128, incorporated by reference in its entirety.
- (b) Support for the amendments to claims 1 and 7 reciting: “wicking the nicotine to the heating element” may be found at least in paragraphs [0640]-[0642], as mentioned above describing devices in which the fluid storage compartment is in fluid communication with a heater (heating element) and provisional patent application 61/820,128 (illustrating use of eGO-C cartridge which includes a wick).
- (c) Support for the amendment to claims 1 and 13 to recite that “wherein inhalation of the aerosol into a user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in ... a Cmax of over 10 ng/mL on average” may be found at least in paragraph [0290].
- (d) Support for the amendment to claim 13, reciting “wherein the liquid reservoir is connected to the vaporizing component by a wick” may be found at least in paragraph [0642].

Thus, no new matter has been added. Amendment of the claims is not to be considered a dedication to the public of any subject matter.

Claims 1-4, 6-10, 12-18 and 20 are currently under consideration. Reconsideration of these claims is requested in view of the amendments and the following remarks.

Response dated: August 19, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

CLAIM REJECTIONS UNDER 35 U.S.C. § 112

Claims 2, 8 and 15

Claims 2, 8 and 15 currently stand rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

By this response, Applicants have amended claims 2, 8 and 15 to fully address the objections mentioned above (e.g., by amending “organic acid” to “lactic acid”). Thus, this rejection has been fully addressed and rendered moot.

DOUBLE PATENTING

Claims 1-4, 6-10 and 12

Claims 1-4, 6-10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 9,215,895 to Bowen et al. (“Bowen ‘895”) in view of U.S. Patent Application Publication No. 2013/0255702 to Griffith, Jr. et al. (“Griffith”).

The Applicants respectfully disagree.

By this response, independent claims 1, 7 and 13 have been amended, emphasizing the lack of obvious subject matter between pending claims 1-4, 6-10 and 12 and the cited references. Should the Examiner maintain the nonstatutory double patenting rejection but otherwise indicate the claims are allowable, the Applicants will likely file a terminal disclaimer to overcome this rejection; filing such a terminal disclaimer earlier would be premature.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103

Claims 1-4, 6-10, 12-18 and 20 currently stand rejected under 35 U.S.C. § 103 as being unpatentable over Griffith (or alternatively Collett et. al, U.S. 8,881,737, hereafter “Collett”) as evidenced by www.e-cigarette-forum.com’s PG-VG-PEG Discussion Posting (“the PG-VG-PEG Internet Posting”) in view of U.S. Patent Application Publication No. 2014/0261474 to Gonda (“Gonda”) and U.S. Patent Application Publication No. 2009/0151717 to Bowen et al. (“Bowen ‘717”). Collett was raised in the Advisory Action of July 28th, 2016 as an alternative to Griffith.

The pending claims are alleged to be obvious in view of the combination of Griffith or Collett, the PG-VG-PEG Internet Posting, Gonda and Bowen ‘717, because these references, in aggregate, include all of the features recited in the claims.

The Applicants respectfully disagree.

The specific and particular arrangement of these features as recited in the claims is not suggested without the use of impermissible hindsight. Further, compelling evidence of commercial success due to the recited features (secondary considerations) is definitive evidence of non-obviousness.

A. IMPERMISSIBLE HINDSIGHT

The Griffith, or alternatively Collett, reference describes a nicotine formulation in which an organic acid (such as lactic acid) is used as a flavorant; neither reference suggests the recited application of a nicotine formulation including lactic acid in a particular PG/VG carrier solution to form nicotine lactate salt solution for vaporization at low temperature and evoking a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL. Instead, the final Office Action relies on the combination with Gonda to suggest this as “Gonda... teaches that administering an aerosolized, liquid nicotine-containing formulation via inhalation (i.e., pulmonary administration) in order to effectuate at peak level of nicotine in the blood plasma...can be accomplished.” (final Office Action, page 9). The final Office Action points to a list of allegedly “results-effective” variables in Gonda involving only routine experimentation to accomplish this recited feature.

Applicants respectfully disagree. Without the use of hindsight, one of skill in the art would not chose a lactic acid formulation from out of the various formulations suggested by Griffith and Collett (which are primarily directed to novel vaporization devices that only very broadly a large variety of vaporization formulations). The results-oriented variables identified by Gonda are not in fact, responsible for the recited Tmax and Cmax features recited in the Applicants' claims. Although Gonda provides a long list of factors that may affect the rate of absorption (e.g., Tmax), including: amount or concentration of nicotine, pH, duration of particle generation, and particle size (see Gonda [0032], [0064] and [0099]), none of these variables are sufficient to achieve the Tmax and Cmax effect recited in the Applicant's claims. As described in the Applicants' specification, it is the unexpected combination of nicotine, lactic acid, and PG/VG in a liquid solution that is vaporized by heating between 100 and 300 °C and inhaled to provide a Tmax of between 3-8 min (and a Cmax over 10 ng/mL). While Gonda suggests that for some formulations could be tweaked by adjusting pH and/or particle size to modify their absorption, Gonda does not show the recited Tmax levels are actually achieved. This is because, as described in the Applicant's disclosure, particle size and pH (and any of the other factors mentioned by Gonda) are not sufficient by themselves, to achieve the proper Tmax, particularly when wicking a liquid reservoir onto a heater that is heated between 100-300 °C to vaporize. Importantly this ability to achieve the target Tmax with a nicotine formulation is not dependent on mere pH, but surprisingly depends on the type of acid included in the formulation, which was not known in the art until the Applicant's invention. The variables referenced by Gonda (e.g., nicotine concentration, pH, etc.) alone or in combination are not sufficient. As Applicants have described, the type of organic acid (including, in particular, lactic acid) is also critical.

Without this essential knowledge, or without the use of hindsight, it cannot be obvious to modify the Griffith reference to achieve the recited Tmax and Cmax values, even if Gonda suggests that it may be beneficial. Although the Office Action asserts that it would be routine for one of skill in the art, given the known "results oriented parameters" of Gonda (e.g., pH, nicotine concentration, particle size) to modify Griffith to achieve the claimed Tmax features, since only "routine experimentation would be needed" to optimize these variables to achieve the "recognized result" (see, e.g., Office Action, page 10). Applicants disagree. The variables being

‘optimized’ in the instant claims are not the same as the variables identified as “results oriented” variables by Gonda. Instead, these variables are the liquid mixture, containing nicotine, the correct carrier mixture (PG/VG) and correct acid (e.g., lactic acid). In order to be obvious for optimization, a variable (or as here, a combination of variables) must be *recognized* as a results-effective variable in the prior art. See, e.g., *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In this case, none of these variables were recognized by the Gonda as relevant to the desired result (e.g., a Tmax of nicotine in the plasma between 3 and 8 minutes), and therefore it could not be obvious to optimize to achieve them. The “results oriented variables” cited by the Office Action in reference to Gonda (e.g., pH, particle size, nicotine concentration) are irrelevant if the wrong acid and therefore salt is generated (e.g., see paragraph [115] “... not all nicotine salts perform similarly to each other or to a traditional cigarette with respect to the rate of nicotine uptake in the blood at early time periods (0-1.5 minutes). These results are unexpected.”). Without knowing what variables must be optimized (e.g., which acid and therefore nicotine salt to use), it could not be obvious to optimize the combination Griffith and Gonda together or with any other reference.

MPEP § 2142 states that “impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art” (emphasis added). “Any judgment on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant’s disclosure, such a reconstruction is proper” (MPEP § 2145(X)(A), quoting *In re McLaughlin*, 443 F.2d 1392, 1395 (CCPA 1971). In this case, the Office Action has use the teachings of the Applicants’ disclosure, showing that the recited composition of nicotine lactate can be optimized to mimic the Tmax and Cmax of traditional tobacco, to select the particular composition from Griffith or Collett for combining with Collette. Without the Applicants’ disclosure, there is no suggestion to combine Griffith and Collett.

B. SECONDARY CONSIDERATIONS

In addition to the arguments presented above, Applicants hereby submit a Rule 1.132 Declaration to present evidence of commercial success and long-felt but unsolved needs that together weigh against a finding of obviousness.

Objective indicia of nonobviousness play a critical role in the obviousness analysis. They are “not just a cumulative or confirmatory part of the obviousness calculus but constitute[] independent evidence of nonobviousness.” *Ortho–McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008). Objective indicia “can be the most probative evidence of nonobviousness in the record, and enables the court to avert the trap of hindsight.” *Crocs, Inc. v. Int’l Trade Comm’n*, 598 F.3d 1294, 1310 (Fed. Cir. 2010) (internal quotation marks omitted). In particular, the objective indicia of nonobviousness are crucial in avoiding the trap of hindsight when reviewing, what otherwise seems like, a combination of known elements.

Applicants respectfully submit that the claimed invention, as supported by the attached declaration under 37 C.F.R. § 1.132, has had great commercial success directly resulting from the incorporation of the all of the features of the claimed invention.

The Supreme Court has recognized commercial success as a possible determinant of patent validity since 1876. *Smith v. Goodyear Dental Vulcanite Co.*, 93 U.S. 486, 495-96 (1876). In 1966, with the landmark decision of *Graham v. John Deere Co.*, the Court reaffirmed the vitality of secondary considerations “[a]s indicia of obviousness or nonobviousness.” (*Graham v. John Deere Co.*, 383 U.S. 1, 17-18). The Court listed commercial success as the first secondary consideration. The commercial success of a product is highly probative of obviousness where the commercial success is attributable to the claimed features that are allegedly obvious; if a product commercially successful product was obvious to invent, then other competitors likely would have already developed it and the market for subsequent entrants to achieve commercial success would be depleted. The potential for achieving commercial success is thought to drive inventors to formulate solutions to existing problems to satisfy marketplace demands. Such evidence of commercial success may help prevent improper hindsight bias when comparing the claimed invention to a combination of prior art.

Prior to the Applicants' invention, existing electronic cigarettes for delivering nicotine to a user did not include a nicotine formulation comprising nicotine, lactic acid, and a carrier of propylene glycol and 90%-30% vegetable glycerol that was vaporized so that inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min. A new vaporizer product incorporating all of the features recited in the Applicants' claims in the fall of 2015. In the eight months since its introduction, this product has exhibited nearly exponential sales growth. This commercial success is directly attributable to the features claimed by the Applicant's claims.

Attached hereto is a 37 C.F.R. § 1.132 Declaration by Dr. Gal Cohen. Dr. Cohen's declaration describes the NJOY Daily commercial electronic cigarette product, a low-temperature vaporizer (electronic cigarette). Neither the Applicants nor Dr. Cohen are affiliated with the NJOY Daily product. The NJOY Daily product incorporates all of the features recited in the claims. As established in Dr. Cohen's declaration and the associated exhibits, sales of the NJOY Daily product have grown rapidly since its introduction, eclipsing the sales of other electronic cigarettes, including other newly introduced and heavily advertised products that do not include the recited features. This commercial success is directly attributable to the claimed features, including in particular, the use of a nicotine mixture including lactic acid and PG/VG, and the ability to achieve a Tmax within approximately the same time as a traditional cigarette (e.g., "wherein inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min") and a Cmax of greater than 10 ng/mL.

(a) The NJOY Daily product includes all of the features recited in the claims

Paragraphs 7 and 8 of Dr. Cohen's exhibit establish that the NJOY Daily electronic cigarette embodies all of the features recited in the claims. The NJOY product is an electronic cigarette including a liquid reservoir; a nicotine formulation within the liquid reservoir, in which the nicotine formulation includes: nicotine lactate (nicotine and lactic acid), and a carrier including propylene glycol and 90%-30% vegetable glycerol. The concentration of nicotine in the nicotine formulation is 4.5% (between 0.5% to about 20%) w/w. The fluid storage

compartment is connected to a heating element by a wick. In operation, the NJOY Daily device produces an aerosol from the nicotine formulation by heating at least a portion of the nicotine formulation between 100°C and 300°C so that inhalation of the aerosol into a user's lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL. This is explicitly shown for the NJOY Daily product in Exhibit G ("Nicotine Delivery" graph).

(b) The NJOY Daily Product has Been Commercially Successful Because It Includes the Features Recited in the Applicants' Claims.

The NJOY Product has enjoyed commercial success which has increased since its introduction into the market in the fall of 2015, as described by Dr. Cohen in detail in paragraphs 5 and 6. For evidence of commercial success to be probative of non-obviousness, there must be a nexus between the commercial success and the features recited in the claims. There are multiple lines of evidence showing that the commercial success of the NJOY Daily product is due (at least in part) to the feature recited in the claims. First, the NJOY Daily product has been specifically advertised as including the features recited in the claims, identifying these features key selling points to consumers. Second, consumer self-reporting data (testimonials) indicate that consumers are purchasing the NJOY daily product precisely because it includes the features recited in the claims. Finally, the company selling the NJOY Daily device (NJOY Inc.) has itself stated that the recited features, in particular the Tmax properties ("nicotine absorption") are at responsible for the commercial success. These points are all described in paragraphs 9-11 of Dr. Cohen's declaration.

Although in many cases it may be difficult to attribute commercial success to particular recited features and not simply advertising (see, e.g., MPEP §716.03(B), citing *Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 227 USPQ 766 (Fed. Cir. 1985)), that is not the case where, as here, the recited features are what is being advertised. Advertisements for the NJOY Daily product explicitly touted the claimed features as selling points to the consumer. Thus, the success of this advertisement campaign itself hinged on the recited features into the NJOY Daily product. See the Declaration of Dr. Gal Cohen, Exhibits F and G. As shown in electronic and print advertisements marketed to consumers and distributors, the NJOY Daily product was

explicitly described as embodying the Applicants claimed features. For example, the NJOY Daily product was described as including nicotine solution including 4.5% nicotine, lactic acid, and 50/50 PG/VG that can provide “over 90%” of the satisfaction as a cigarette “during the first seven minutes,” based on a “clinical trial conducted by [an] independent lab measuring nicotine absorption in blood stream [Tmax]...”. Some advertisements went so far as to include a graph showing the Tmax and Cmax values for the NJOY Daily (compared to other products and a traditional cigarette) as shown by the flyer in Exhibit G.

The nexus between the recited features, including the nicotine solution with nicotine, lactic acid and PG/VG that results in a nicotine plasma Tmax from about 3 minutes to about 8 min and a Cmax of over 10 ng/mL, is also shown by consumer testimonials (Exhibit H of Dr. Cohen’s declaration). Consumers have self-reported that they purchase and prefer the NJOY Daily product because of the recited features, compared to other commercial products that do not include these features. The rapid blood absorption (Tmax) is typically expressed by consumers as a nicotine satisfaction or “fix” similar or identical to traditional cigarettes.

Finally, as shown in Exhibit A of Dr. Cohen’s Declaration, the company offering the NJOY Daily product (NJOY, Inc.) directly attributes the commercial success to the rapid blood absorption (Tmax) (“NJOY attributes the Daily’s early success to the product’s accessible \$5.99 MSRP, as well as its ability to create a bridge to familiarity for adult smokers through its lightweight, soft touch design *and superior nicotine absorption.*”).

In light of the strong and unambiguous evidence of commercial success, which is directly attributable to the recited features of the Applicants’ claims, as shown in the attached 37 C.F.R. § 1.132 Declaration and discussed above, the Applicant’s respectfully request withdrawal of the 35 U.S.C. § 103 rejection of claims 1-4, 6-10, 12-18 and 20 and allowance of all of the currently pending claims.

Response dated: August 19, 2016
App. No.: 14/925,968; Filed: October 28, 2015
Response to Office Action of May 13, 2016

CONCLUSION

In light of the remarks set forth above, Applicants respectfully request the Examiner expedite the prosecution of this patent application to issuance. If it is determined that a telephone conference would aid in the prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 287-2164.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-4050** referencing docket no. 13211-713.303. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Date: August 19, 2016

Respectfully submitted,



Richard D. Shoop
Registration No. 45,763

SHAY GLENN LLP
2755 CAMPUS DRIVE, SUITE 210
SAN MATEO, CA 94403
TELEPHONE: 650.287.2164
FACSIMILE: 650.212.7562

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
Inventor(s) : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND
METHODS THEREOF
Customer No. : 66854

DECLARATION UNDER 37 C.F.R. § 1.132

I, Dr. Gal Cohen, declare as follows:

- (1) I hold a PhD in Molecular and Cellular Physiology from Stanford University.
- (2) I am the Head of Scientific and Regulatory Affairs at PAX Labs, Inc. ("PAX"), a market leader in vaporization (including electronic cigarette) technology, where I have been employed or affiliated since 2008.
- (3) PAX Labs is the applicant and owner of U.S. patent application no. 14/925,968, for which this declaration is being submitted.
- (4) As part of my employment at PAX, I monitor the sales and marketing of other electronic cigarette manufacturers, including NJOY, Inc.
- (5) In or around September of 2015, NJOY, Inc. released a new product, called the "NJOY Daily". Since its introduction, sales of the NJOY Daily product have grown substantially and the NJOY Daily has experienced a significant commercial success, particularly as compared to other electronic cigarettes. Exhibit A, attached hereto is a copy of an article from the June 10, 2016 edition of "Convenience Store Decisions." The article, dated March 30, 2016, is entitled "NJOY Daily E-Cig Sales Soar." As reported in the article, the NJOY Daily "is currently the fastest turning new e-vapor product, outselling other new products such as JTI's Logic Pro and Pax Labs' JUUL."
- (6) I have also monitored the sales of the NJOY Daily product using Information Resources, Inc. (IRI), a syndication service that tracks consumer product sales and marketing. IRI analysis of NJOY, Inc. shows that since its introduction, 4 week sales in all convenience store channels of NJOY Daily have grown from \$0 a year ago to just

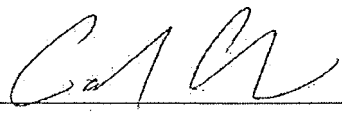
under a million dollars (\$908,604). In the same time period, sales of other, established NJOY, Inc., products (including “NJOY Vaping” and “NJOY Bold”) have decreased in sales by an aggregate of just over \$700,000. This data is shown in Exhibit B. NJOY, Inc. has included a graphic illustrating unit sales of the NJOY Daily product as part of its advertisement material promoting the product to distributors, which is shown in Exhibit C. The graphic shows the exponential growth of NJOY Daily sales based on IRI data using four week sales data for sales in all channels ending on January 3, 2016.

- (7) I have purchased and examined the NJOY Daily product. The NJOY Daily embodies all of the features of the pending claims of the U.S. patent application no. 14/925,968. The NJOY Daily is an electronic cigarette that includes a liquid nicotine formulation of nicotine, lactic acid, and a carrier of 50/50 propylene glycol (PG) and vegetable glycerin (VG). Exhibit D, attached hereto, is a description of the NJOY Daily product that is provided on the NJOY website (www.njoy.com/faq, last visited June 10, 2016). I have also requested and reviewed a chemical analysis of the liquid nicotine composition of a purchased NJOY Daily product, and have confirmed that the composition of this product is the same as recited in the claims of U.S. patent application no. 14/925,968. Specifically, the NJOY Daily nicotine formulation is a liquid solution of nicotine (between 46.8 and 47.3 mg/mL) and lactic acid (between 22.6 and 22.4 mg/mL) with a biologically acceptable liquid carrier of propylene glycol and glycerin (vegetable glycerol). The vegetable glycerol is between 90% and 30% of the liquid carrier. The chemical analysis was performed by a commercial chemical lab, Enthalpy Analytical, Inc., and a copy of this report is attached as Exhibit E. The liquid solution of the NJOY Daily product saturates a sponge that is held within a fluid storage compartment, and the liquid solution within the storage compartment is connected to a heating element by a wick. During operation of the NJOY Daily product, the nicotine formulation is wicked from the fluid storage compartment to the heating element and heated to between about 100°C and about 300°C to generate an inhalable aerosol.
- (8) The use of the NJOY Daily product also results in the nicotine plasma Tmax from about 3 min to about 8 minutes and a Cmax of over 10 ng/ml when the aerosol produced by the NJOY Daily is inhaled into the user’s lungs over a period of about 5 minutes at a rate of about one inhalation per 30 seconds. Exhibit G shows an example of advertising material promoting the NJOY Daily product which describes the product as “over 90 percent as satisfying as a cigarette during the first 7 minutes of use,” based on the Tmax and Cmax profile for the NJOY Daily. In Exhibit G, the statements referring to the increased satisfaction in strength and timing of the nicotine delivery refer to a clinical trial “conducted by [an] independent lab measuring nicotine absorption in [the] blood stream represented by mean of test subjects assessed on day 8 of use following 12 hours of abstinence.” Exhibit F shows two screen captures of the advertisement aimed at consumers for the NJOY Daily that describe the peak blood nicotine concentration (Tmax) occurring within the first seven minutes of use, which is describes as providing a satisfaction similar to what is achieved by a traditional cigarette. In addition, the Tmax and Cmax resulting from the NJOY Daily product is also described in advertising material targeting distributors, as shown in Exhibit G. Exhibit G is an advertising flyer distributed by NJOY Inc, targeting distributors and

customers of NJOY Daily. In Exhibit G, the graph titled “Nicotine Delivery” at the bottom right shows that the NJOY Daily has a Tmax between 3 minutes and 8 minutes, and a Cmax of greater than 10 ng/ml (mean nicotine concentration). The “Chart Notes” provided at the bottom of the flyer indicate that the graph represents a “[c]linical trial conducted by independent lab measuring nicotine absorption in blood stream represented by mean of test subjects assessed on day 8 of use following 12 hours of abstinence. N=18-20 per product. Subjects smokers aged 18-65 not currently attempting to quit. Products puffed (starting at time zero) every 30 seconds for 5 minutes.”

- (9) It is my opinion that the commercial success of the NJOY Daily product is attributed to the features recited in the claims of U.S. patent application no. 14/925,968. The Tmax and Cmax values of the NJOY Daily product which result from the nicotine solution including nicotine, lactic acid and the PG/VG carrier provide a cigarette-like satisfaction. The rapid onset (e.g., Tmax between 3 and 8 minutes) of a relatively high blood nicotine level (e.g., Cmax over 10 ng/mL) result in a user experience and satisfaction that is closer to the experience provided by a traditional cigarette. It has long been the goal of electronic cigarette manufactures to provide an electronic cigarette that can mimic the experience of a traditional cigarette, because of the potential for tremendous commercial success. There are numerous user-reported testimonials available online in which users discuss their reasons for purchasing the NJOY Daily product; the majority of such self-reporting comments refer to the cigarette-like experience that it provides.
- (10) In addition, the features recited in the claims, and particularly the Tmax and Cmax profiles, are used extensively in the NJOY Daily marketing and advertisement materials to drive consumer purchases. For example, the consumer advertisements show in Exhibit F tout the Cmax and Tmax properties as providing a user experience that is most similar to cigarettes. In Exhibit F, on the top left (“Meet NJOY Daily”), the advertisement claims that “over 90 percent as satisfying as a cigarette,” and on bottom of (“IT’S THAT SATISFYING”), a similar advertisement states “[o]ur latest innovation is now delivering the most authentic ‘smoking’ experience to date. We’re proud (and really freakin excited) to introduce the Daily – a labor of love that blends Satisfaction, Performance, Authenticity, Flavor and Design for an experience that’s more than 90% as satisfying as a cigarette during the first 7 minutes of use.” The advertisement of Exhibit G is even more explicit, graphically showing the Tmax and Cmax curves and describing the NJOY Daily as providing “[q]uick & strong satisfaction more like a cigarette”.
- (11) Finally, the NJOY company itself credits the nicotine absorption into the blood, the Tmax and Cmax properties of the NJOY Daily, as at least partially responsible for the commercial success. The recent article (“NJOY Daily E-Cig Sales Soar”) in Exhibit A cites NJOY as attributing the early success of the NJOY Daily product to “its lightweight, soft touch design and superior nicotine absorption.”
- (12) I declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further that these

statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under the provisions of 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of any patent issuing upon U.S. Application Serial No. 14/632,161, or any continuing application thereof.

Signature: 
Gal A. Cohen, PhD

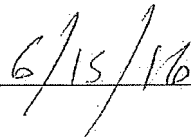
Date: 
6/15/16

EXHIBIT A

Convenience
Store
Decisions

June 10, 2016

TOP STORIESNEW PRODUCTS C-STORE TRENDSCHAIN OF THE YEARCATEGORY NEWS & DATA RACK PRICING

[Home](#) » [Recent CSD Articles](#) » [Categories](#) » [Today's News](#) » NJOY Daily E-Cig Sales Soar

NJOY Daily E-Cig Sales Soar

March 30, 2016 [CSD Staff](#) : [0 Comments](#)



Accessible pricing and lightweight, soft touch design help spur consumer demand for NJOY Daily.

E-cigarette manufacturer NJOY shared the latest IRI FDMxC ("All-Channel") data, revealing that the NJOY Daily disposable e-cig is currently the fastest-turning new e-vapor product, outselling other new products such as JTI's Logic Pro and Pax Labs' Juul.

The data indicates that NJOY Daily is finding a home in the hands of adult smokers looking for an introductory e-vapor product that delivers nicotine satisfaction more like a cigarette.

According to IRI data, NJOY Daily's 3 SKUs moved more than 37,000 units in the single week ending Feb. 21, 2016. This amounts to 23% greater unit sales per week when compared with Logic Pro and 281% greater unit sales per week than Juul.

NJOY attributes Daily's early success to the product's accessible \$5.99 MSRP, as well as its ability to create a bridge to familiarity for adult smokers through its lightweight, soft touch design and superior nicotine absorption. Thanks to their valued retail partners, NJOY has been able to leverage promotional support, merchandising, signage, and marketing assets to drive trial among adult smokers.

An early e-vapor pioneer, NJOY is currently the largest independent e-cigarette and vaping company in the USA. NJOY has heavily invested in R&D and market studies to further its ongoing commitment to product innovation based on consumer research and leading-edge science.

EXHIBIT B
IRI Data

NJOY, Inc. sells 3 product lines:

- (1) NJOY vaping (vape pen and e-liquid bottles with a traditional nicotine formulation)
- (2) NJOY Bold (cigalikes with a traditional nicotine formulation)
- (3) NJOY Daily (cigalike with a lactic acid based formulation)

Based on data provided by Information Resources, Inc (IRI), in the past year, 4 week sales in all convenience store channels for all NJOY products have increased from \$2,079,734 to \$2,274,610. However, the proportion of sales represented by NJOY Daily has increased from 0% to 40%, while sales of all other products (NJOY vaping and NJOY Bold) have decreased by 60%.

	4 weeks ending 5/15/16		year ago		change y/y
vaping	\$879,301	39%	\$1,015,091	49%	(\$135,789)
Bold	\$486,705	21%	\$1,064,644	51%	(\$577,939)
Daily	\$908,604	40%	\$0	0%	\$908,604
Total	\$2,274,610		\$2,079,734		\$194,876

INTRODUCING NJOY[®] DAILY

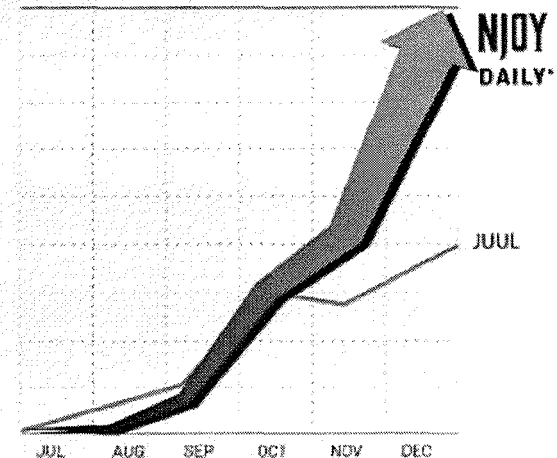
THE DIFFERENTIATED DISPOSABLE

DESIGNED WITH RETAILERS IN MIND

REINVIGORATING CONSUMER TRIAL	<ul style="list-style-type: none"> • Everyday value - approximately 300 puffs for \$5.99 per stick • Quick & strong satisfaction more like a cigarette • Disposable lightweight stick
MAXIMIZE PURCHASE FREQUENCY & PROFITS	<ul style="list-style-type: none"> • ~40% margins* • 1 count configuration to maximize purchase frequency • Compact 5 count cartons for limited investment and optimal turns • Flavor freshness seal for extended shelf life • ~70% higher gross profit per week vs. leading rechargeable refills**
SELL THROUGH RATE SUPPORT	<ul style="list-style-type: none"> • Multi-million dollar consumer advertising campaign • Robust introductory price promotions • Modular merchandising displays and impactful signage • Trial generating activations • Targeted coupon delivery to adult smokers

**REINVIGORATING
CONSUMER TRIAL**
BY DELIVERING SATISFACTION
MORE LIKE A CIGARETTE.

IRI UNIT SALES
ALL CHANNEL***



Source:

*Assumes average MSRP and cost of NJOY kit price

**Assumes \$2.74 Gross Profit per leading rechargeable 300 puff and assumes 7 units per week of consumption. "1 Day" Definition: Disposable = 1 stick;

Recharge = 1 cartridge. Assumes 1 unit purchased per store visit.

***IRI 4 Weeks Ending 12/31/16 All Channel = TDNA + C-Store



EXHIBIT D

Screen captures from www.njoy.com/faq (taken 6/10/2016):

What is e-liquid?

The main ingredients by volume in NJOY's vape e-liquids are propylene glycol (PG) and vegetable glycerin (VG). The secondary ingredients are nicotine and flavors.

All of NJOY's e-liquids are made in the USA with domestic and imported ingredients, and contain pharmaceutical grade PG, VG and nicotine. The e-liquid in the following products also contain lactic acid: NJOY Daily (all flavors) and our Classic Tobacco and Menthol vaping e-liquids.

NJOY Vape e-liquids contain 50% vegetable glycerin (VG) and 50% propylene glycol (PG).

The VG/PG ratios in the Artist Collection:

Paramour: 50/50 Hedon's Bite: 60/40 Sacré Coeur: 50/50 Dragon Scape: 70/30 Samba Sun: 60/40

Daily, the disposable e-cig that offers the most authentic 'smoking' experience is available in Rich Tobacco, Cool Menthol, Blue + Black Berry and Classic Tobacco (online only...coming soon).

Kings, the disposable e-cig that started it all, comes in bold, gold and menthol flavors.

Recharge comes in a range of flavors beyond menthol and traditional, including vanilla bean and pomegranate.

NJOY Vaping e-liquids come in a wide variety of flavors. You can see the all here.

Artist Collection is an exclusive line of complex e-liquids crafted by five leading artists in the vape industry in partnership with NJOY.

Check out all of our flavor chambers and e-liquids today.

How much nicotine is in NJOY products?

Ask and you shall receive:

NJOY Daily

- Rich Tobacco: 4.5% nicotine by weight
- Cool Menthol: 4.5% nicotine by weight
- Blue + Black Berry: 4.5% nicotine by weight

Some of your products now list lactic acid in the ingredient list, why?



Lactic acid is used in certain products to optimize the throat hit as well as your overall experience.

What is the difference between the NJOY King and the NJOY Daily?



There are several differences between the King and Daily, besides its size. NJOY Daily has been innovated to deliver quick & strong satisfaction more like a cigarette, it features a new longer lasting battery with QuickVapor technology delivering significantly longer battery life (approx. 300 puffs), has new upgraded flavors, more vapor volume and a discreet but stylish new design.

EXHIBIT E

PAX Labs, Inc.

660 Alabama Street, Second Floor
San Francisco, CA 94110

E-Liquid Analysis

Electronic Cigarette (eC) Liquid Testing

Analysis Report
(1115-553)

GC/FID Analysis (ENT184)

Nicotine, Propylene glycol, Vegetable glycerin, Water

HPLC/UV Analysis (ENT301-Mod)

Lactic Acid



Enthalpy Analytical, Inc.

Phone: (919) 850 - 4392 / Fax: (919) 850 - 9012 / www.enthalpy.com
800-1 Capitola Drive Durham, NC 27713-4385

I certify that to the best of my knowledge all analytical data presented in this report summary :

- Have been checked for completeness
- Are accurate, error-free, and legible
- Have been conducted in accordance with approved protocol

This analytical report was prepared in Portable Document Format (.PDF) and contains 10 pages.

Jennifer B. Feller

QA Review Performed by: Jennifer B. Feller

Report Issued: 1/6/2016



Summary of Results





Report for: PAX Labs, Inc.
Client Project: Electronic Cigarette (eC) Liquid Testing
Sample Type: e-Liquid

Project Code: 1115-553
Project Start Date: 11/13/15
Analysis Method: ENT184

Enthalpy Code	Client Code	Nicotine (mg/mL)	Propylene glycol (mg/mL)	Glycerin (mg/mL)	Water # (mg/mL)
1115-553-01-01	PO-J1-1511112A1	46.8	491	487	57.6
1115-553-01-02		47.3	497	489	59.9

#: Water results are blank corrected.

Report for: PAX Labs, Inc.
 Client Project: Electronic Cigarette (eC) Liquid Testing
 Sample Type: e-Liquid

Project Code: 1115-553
 Project Start Date: 11/13/15
 Analysis Method: ENT301-Mod

Enthalpy Code	Client Code	Notes	Lactic Acid (ug/mL)
1115-553-01 (DF 1010) 1	PO-J1-1511112A1	--	22,597
1115-553-01 (DF 1010) 2			22,389
		Average	22,493
		%DIFF	0.9

Narrative Summary



Enthalpy Analytical Narrative Summary

Company	PAX Labs, Inc.
Analysts	KEH, BJB/ABP
Parameters	ENT184, ENT301-Mod

Client Proj	Electronic Cigarette (eC) Liquid Testing
Job #	1115-553
#Samples	1 eC Liquid Sample

Custody	<p>A scintillation vial labeled "<i>E-Liquid test nicotine, Lactic acid PG. Glycerin PO-J1-151112A1</i>" was used for this project. It was prepared and analyzed in duplicate.</p> <p>Prior to, during, and after analysis, the sample was kept under lock with access only to authorized personnel by Enthalpy Analytical, Inc.</p>
ENT184 (Primary Constituents)	<p>The e-Liquid sample was prepared and analyzed in duplicate for nicotine, propylene glycol (PG), and vegetable glycerin (aka VG, glycerin, or glycerol), and water following the analytical procedures in Enthalpy SOP ENT184.</p> <p>The samples were analyzed on the Hewlett Packard Model 6890 Gas Chromatograph "BMO" equipped with a Flame Ionization Detector (FID) and an appropriate column.</p>
ENT301-Mod (Lactic Acid)	<p>The e-Liquid sample was prepared and analyzed in duplicate for lactic acid following the general analytical procedures in Enthalpy SOP ENT301.</p> <p>The samples were analyzed using the Agilent Model 1100, High Performance Liquid Chromatograph "Selma," equipped with an Ultraviolet (UV) Detector operating at 360 nm and an appropriate column.</p>
QC Notes	<p>All QC samples were within acceptance criteria unless otherwise noted.</p> <p>As the lactic acid analysis was not a standard laboratory method, a second source standard was not available to verify the calibration for lactic acid. A continuing calibration sample was analyzed after the samples, and had a recovery of 98.7% of the expected concentration.</p>
Reporting Notes	<p>Sample and calibration curve chromatograms are available upon request.</p> <p>The results presented in this report are representative of the samples as provided to the laboratory.</p>



General Reporting Notes

The following are general reporting notes that are applicable to all Enthalpy Analytical, Inc. data reports, unless specifically noted otherwise.

- Any analysis which refers to the method as “*Type*” represents a planned deviation from the reference method. For instance a Hydrogen Sulfide assay from a Tedlar bag would be labeled as “EPA Method 16-Type” because Tedlar bags are not mentioned as one of the collection options in EPA Method 16.
- The acronym **MDL** represents the Minimum Detection Limit. Below this value the laboratory cannot determine the presence of the analyte of interest reliably.
- The acronym **LOQ** represents the Limit of Quantification. Below this value the laboratory cannot quantitate the analyte of interest within the criteria of the method.
- The acronym **ND** following a value indicates a non-detect or analytical result below the MDL.
- The letter **J** in the Qualifier or Flag column in the results indicates that the value is between the MDL and the LOQ. The laboratory can positively identify the analyte of interest as present, but the value should be considered an estimate.
- The letter **E** in the Qualifier or Flag column indicates an analytical result exceeding 100% of the highest calibration point. The associated value should be considered as an estimate.
- The acronym **DF** represents Dilution Factor. This number represents dilution of the sample during the preparation and/or analysis process. The analytical result taken from a laboratory instrument is multiplied by the DF to determine the final undiluted sample results.
- The addition of **MS** to the Sample ID represents a Matrix Spike. An aliquot of an actual sample is spiked with a known amount of analyte so that a percent recovery value can be determined. The MS analysis indicates what effect the sample matrix may have on the target analyte, i.e. whether or not anything in the sample matrix interferes with the analysis of the analyte(s).
- The addition of **MSD** to the Sample ID represents a Matrix Spike Duplicate. Prepared in the same manner as an MS, the use of duplicate matrix spikes allows further confirmation of laboratory quality by showing the consistency of results gained by performing the same steps multiple times.
- The addition of **LD** to the Sample ID represents a Laboratory Duplicate. The analyst prepares an additional aliquot of sample for testing and the results of the duplicate analysis are compared to the initial result. The result should have a difference value of within 10% of the initial result (if the results of the original analysis are greater than the LOQ).
- The addition of **AD** to the Sample ID represents an Alternate Dilution. The analyst prepares an additional aliquot at a different dilution factor (usually double the initial factor). This analysis helps confirm that no additional compound is present and coeluting or sharing absorbance with the analyte of interest, as they would have a different response/absorbance than the analyte of interest.
- The Sample ID **LCS** represents a Laboratory Control Sample. Clean matrix, similar to the client sample matrix, prepared and analyzed by the laboratory using the same reagents, spiking standards and procedures used for the client samples. The LCS is used to assess the control of the laboratory’s analytical system. Whenever spikes are prepared for our client projects, two spikes are retained as LCSs. The LCSs are labeled with the associated project number and kept in-house at the appropriate temperature conditions. When the project samples are received for analysis, the LCSs are analyzed to confirm that the analyte could be recovered from the media, separate from the samples which were used on the project and which may have been affected by source matrix, sample collection and/or sample transport.



General Reporting Notes

(continued)

- **Significant Figures:** Where the reported value is much greater than unity (1.00) in the units expressed, the number is rounded to a whole number of units, rather than to 3 significant figures. For example, a value of 10,456.45 ug catch is rounded to 10,456 ug. There are five significant digits displayed, but no confidence should be placed on more than two significant digits.
- **Manual Integration:** The data systems used for processing will flag manually integrated peaks with an "M". There are several reasons a peak may be manually integrated. These reasons will be identified by the following two letter designations. The peak was *not integrated* by the software "NI", the peak was *integrated incorrectly* by the software "II" or the *wrong peak* was integrated by the software "WP". These codes will accompany the analyst's manual integration stamp placed next to the compound name on the chromatogram.



**This Is The Last Page
Of This Report.**



EXHIBIT F

MEET NJOY DAILY

Over 90 percent as satisfying as a cigarette*



Strong throat hit for authentic feel

Flavors formulated & blended in a pharmaceutical-grade facility in the USA



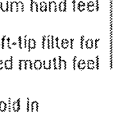
Flavor concentration increased for maximum satisfaction

FEEL THE DIFFERENCE



Soft touch wrapper for premium hand feel

Soft-tip filter for enhanced mouth feel



Small & light enough to hold in your mouth or in two fingers

INNOVATIVE DESIGN

New QuickVapor technology battery delivers vapor faster and extends battery life to approximately 300 puffs (~ 1 pack of cigarettes)



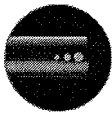
50/50 PG/VG balance to maximize vapor thickness and volume

STYLE & SUBSTANCE

Tip illuminates to let you know it's on without being conspicuous



Tone-on-tone logo adds discreet sophistication



Food-grade coloring on the mouth tip for style & safety

Color dots are a subtle flavor reminder

*During the first seven minutes. Clinical trial conducted by independent lab measuring nicotine absorption in blood stream represented by mean of test subjects assessed on day 6 of use following 12 hours of abstinence; measured using participating subject's preferred brand of cigarette.



IT'S THAT SATISFYING

Our latest innovation is now delivering the most authentic "smoking" experience to date. We're proud (and really freakin' excited) to introduce the Daily – a labor of love that blends Satisfaction, Performance, Authenticity, Flavor and Design for an experience that's more than 90% as satisfying as a cigarette during the first 7 minutes of use.

*June 2015 in-home consumer study consisting of adult smokers using tobacco and menthol flavor of both brands.

(Screen capture from <https://www.njoy.com/daily>, last visited June 13, 2016)

EXHIBIT G

INTRODUCING NJOY® DAILY THE DIFFERENTIATED DISPOSABLE

DESIGNED WITH RETAILERS IN MIND

REINTEGRATING CONSUMER TRIAL

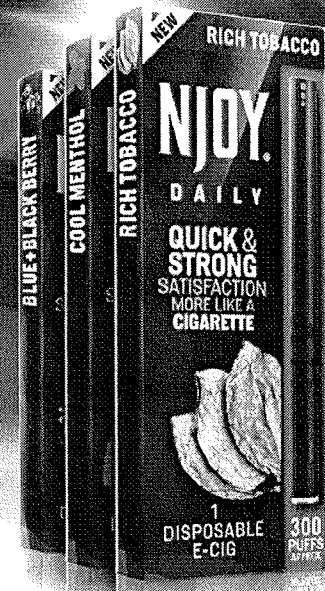
- Everyday value - approximately 300 puffs for \$5.99 per stick
- Quick & strong satisfaction more like a cigarette
- Disposable lightweight stick

MAXIMIZE PURCHASE FREQUENCY & PROFITS

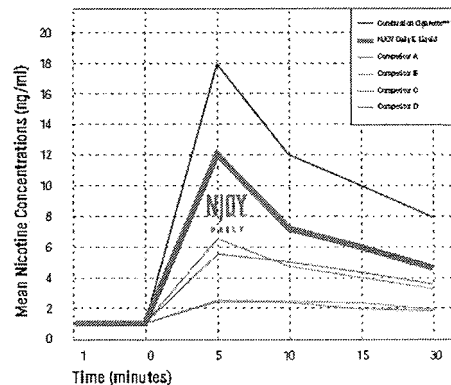
- ~40% margins*
- 1 count configuration to help restore purchase frequency
- Compact 5 count cartons for limited investment and optimal turns
- Flavor freshness seal for extended shelf life
- ~70% higher gross profit per week vs. leading rechargeable refills**

SELL THROUGH RATE SUPPORT

- Robust introductory pricing promotions
- Modular merchandising displays and impactful signage
- Multi-million dollar consumer advertising campaign
- Trial generating activations
- Targeted coupon delivery to adult smokers



NICOTINE DELIVERY
CIGARETTE VS TOP C STORE BRANDS



Source:

*M signifies measure MGR and cost - RDPH 185 price

** Assumes "Committed user": Users completely switching from pack a day of cigarettes to E-Paper Products. Assumes 7 units per week of consumption. 1 Unit Definition: Disposable = 1 stick.

Package: 1 count; 1 E-Cig: 1.4 mg. E-Paper Product assumes 1 unit purchased per visit.

*** Measured as the participating subjects preferred brand of cigarette.

Chart Notes: Clinical trial conducted by independent lab measuring nicotine absorption in blood's stream represented by mean of test subjects measured on day 8 of use following 12 hours of abstinence.

N=18-20 per product. Subjects smokers aged 18-65 not currently attempting to quit. Products puffed (starting at time zero) every 30 seconds for 5 minutes.

WARNING: NJOY® products are not smoking cessation products and have not been tested as such, nor have the long-term effects of using this product been established. NJOY® products are intended for use by adults of legal smoking age (18 or older in California) and not by children, women who are pregnant or breastfeeding, or persons who are at risk of heart disease, high blood pressure, diabetes or taking a medicine for depression or asthma. NJOY® products contain nicotine, a chemical known to the State of California to cause birth defects or other reproductive harm. Nicotine is addictive and habit forming, and it is very deadly if inhaled or in contact with the skin, or if swallowed. Ingestion of the non-vaporized components of the products is the liquid components of NJOY® products can be poisonous. If any liquid is inhaled, seek medical assistance immediately.



EXHIBIT H

Consumer Testimonials

Sampling of customer testimonials from www.njoy.com/ (last visited 6/10/2016)



Julia Verified Reviewer

04/29/16



Love your Daily ecigarette, Blue + black berry

This product is awesome! Really great flavor, really awesome vapor. I would definitely recommend this ecig to a friend who is looking to switch. Best ecig out there by far in terms of nicotine satisfaction!



Sammy G. Verified Reviewer

02/04/16



The njoy Daily is the best e-cigarette yet!

I've tried them all...well most of them. This is the first e-cigarette that really offers an effective substitute to a real cigarette. Terrific!



Sam J. Verified Reviewer

03/07/16



Best E-cigs in the Game!

NJOY is my go-to e-cig.. I was a long time user of the Kings e-cigarette and I've just recently made the switch to their new Daily electronic cigarette.. The Daily e-cig has the nicotine fix I need and it really does feel like a regular cigarette.. The Blue + Black Berry is my favorite flavor !!

Share |

Was This Review Helpful? 4 0

Customer testimonials from <http://www.vaporauthority.com/products/genuine-njoy-daily-disposable-e-cig> (last visited June 10, 2016):

★★★★★ (5/5)

Steven P from **Philly** on **May 17, 2016**

Great disposable here, probably the best one I've ever tried. Got one a while ago just for shits but now I pick a couple of em up every time I place an order here. These are so easy for out and about or stealthy vaping. Damn close to an analog too!

[Report this review](#)

★★★★★ (5/5)

Morgan from **Denver** on **Apr 29, 2016**

Unbelievable! It's like I'm smoking a cigarette again, but I'm not... I have been vaping instead of smoking for like a year now and this is a great way to revisit that without feeling like shit afterwards! Whooo Hoooo!

[Report this review](#)

★★★★★ (5/5)

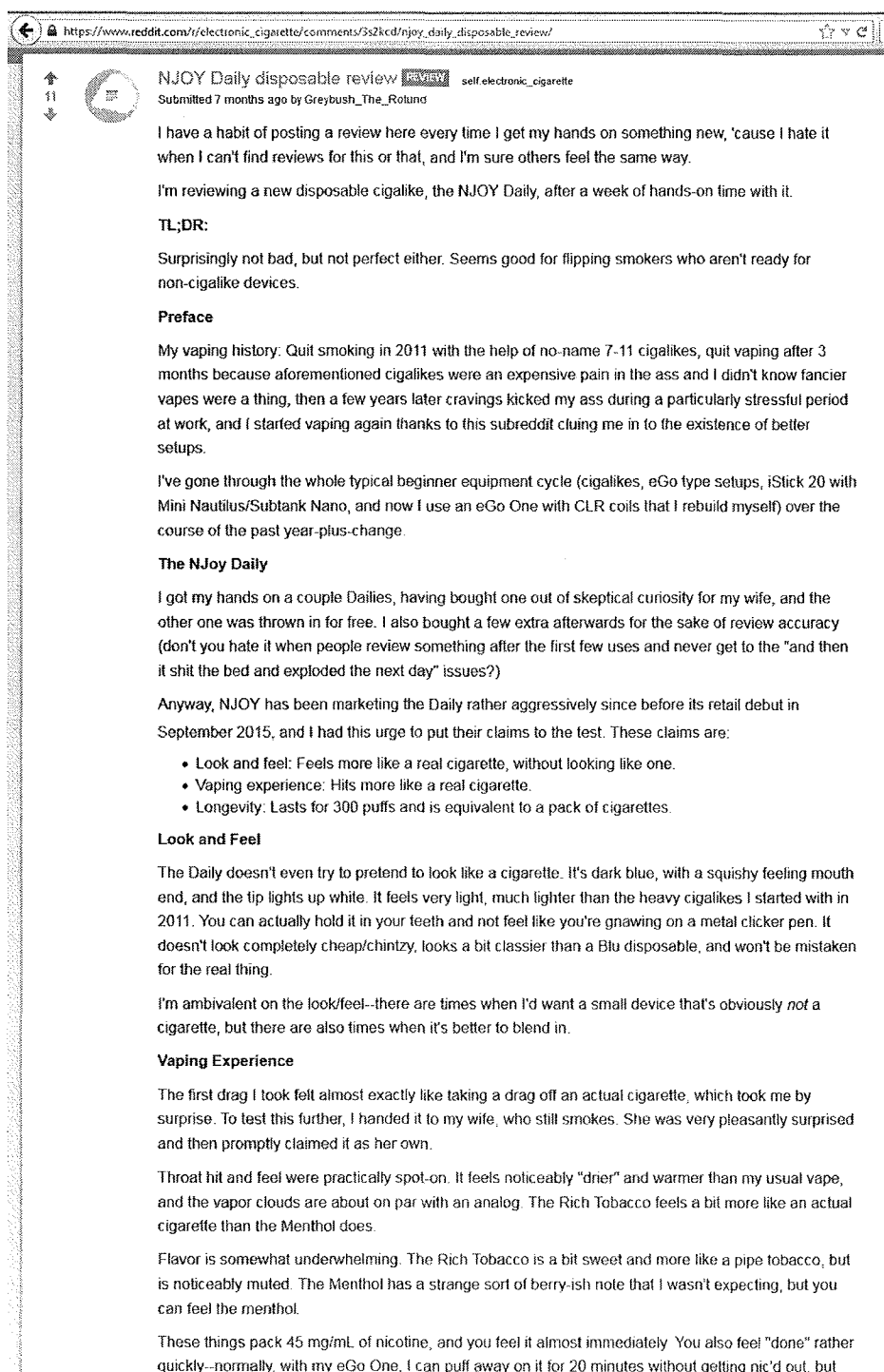
Alana B from **Austin Tx** on **Apr 11, 2016**

Oh Wow! I've tried other ecigs like this from the gas station and they were disappointing, but I'd never seen these Daily before. Now this is the closest thing to a real cigarette that I've ever had! I mean, if its this good I don't know why anyone would smoke real cigs.. Completely satisfying!! I actually have a nice vape set up and I just ordered these out of curiosity and I wanted an emergency go-to if my vape broke or got lost or something. Really good on the out and about. I'm definitely going to keep a stock of these around for rough times. Would be great for someone just trying to quit cigarettes, but it could get costly if you just relied on these. Get these and also a good mod and tank - and your golden! Much appreciated Vapor Authority!

[Report this review](#)

Exemplary Customer review from Reddit:

https://www.reddit.com/r/electronic_cigarette/comments/3s2kcd/njoy_daily_disposable_review/ (last visited June 10, 2016):



↑
f1
↓

NJOY Daily disposable review REVIEW self:electronic_cigarette
Submitted 7 months ago by Greybush_The_Rotund

I have a habit of posting a review here every time I get my hands on something new, 'cause I hate it when I can't find reviews for this or that, and I'm sure others feel the same way.

I'm reviewing a new disposable cigalike, the NJOY Daily, after a week of hands-on time with it.

TL;DR:

Surprisingly not bad, but not perfect either. Seems good for flipping smokers who aren't ready for non-cigalike devices.

Preface

My vaping history: Quit smoking in 2011 with the help of no-name 7-11 cigalikes, quit vaping after 3 months because aforementioned cigalikes were an expensive pain in the ass and I didn't know fancier vapes were a thing, then a few years later cravings kicked my ass during a particularly stressful period at work, and I started vaping again thanks to this subreddit cluing me in to the existence of better setups.

I've gone through the whole typical beginner equipment cycle (cigalikes, eGo type setups, iStick 20 with Mini Nautilus/Subtank Nano, and now I use an eGo One with CLR coils that I rebuild myself) over the course of the past year-plus-change.

The NJoy Daily

I got my hands on a couple Dailies, having bought one out of skeptical curiosity for my wife, and the other one was thrown in for free. I also bought a few extra afterwards for the sake of review accuracy (don't you hate it when people review something after the first few uses and never get to the "and then it shit the bed and exploded the next day" issues?)

Anyway, NJOY has been marketing the Daily rather aggressively since before its retail debut in September 2015, and I had this urge to put their claims to the test. These claims are:

- Look and feel: Feels more like a real cigarette, without looking like one.
- Vaping experience: Hits more like a real cigarette.
- Longevity: Lasts for 300 puffs and is equivalent to a pack of cigarettes.

Look and Feel

The Daily doesn't even try to pretend to look like a cigarette. It's dark blue, with a squishy feeling mouth end, and the tip lights up white. It feels very light, much lighter than the heavy cigalikes I started with in 2011. You can actually hold it in your teeth and not feel like you're gnawing on a metal clicker pen. It doesn't look completely cheap/chintzy, looks a bit classier than a Blu disposable, and won't be mistaken for the real thing.

I'm ambivalent on the look/feel--there are times when I'd want a small device that's obviously *not* a cigarette, but there are also times when it's better to blend in.

Vaping Experience

The first drag I took felt almost exactly like taking a drag off an actual cigarette, which took me by surprise. To test this further, I handed it to my wife, who still smokes. She was very pleasantly surprised and then promptly claimed it as her own.

Throat hit and feel were practically spot-on. It feels noticeably "drier" and warmer than my usual vape, and the vapor clouds are about on par with an analog. The Rich Tobacco feels a bit more like an actual cigarette than the Menthol does.

Flavor is somewhat underwhelming. The Rich Tobacco is a bit sweet and more like a pipe tobacco, but is noticeably muted. The Menthol has a strange sort of berry-ish note that I wasn't expecting, but you can feel the menthol.

These things pack 45 mg/mL of nicotine, and you feel it almost immediately. You also feel "done" rather quickly--normally, with my eGo One, I can puff away on it for 20 minutes without getting nic'd out, but

with the Daily, I'm done within 5-10 minutes.

Hilariously, I also frequently caught myself absentmindedly flicking/tapping it like the real thing.

Short form, it feels and hits like a real cigarette, but falls short in the flavor department.

Longevity

Normally, whenever a cigalike claims that it's equivalent to a whole pack of cigarettes, I usually bust out laughing because I've never gotten anywhere near that kind of performance out of cigalikes in the past.

The "300 puffs" type of marketing statement is also probably based on the work of an unpaid intern with a small squeeze bulb and a click counter. Hardly anyone I know smokes or vapes like a small squeeze bulb, so puff count is a metric that I usually dismiss as irrelevant.

The more practical metric I'd use instead, when judging whether or not a cigalike is equivalent to a pack of cigarettes, starts with how long that pack would last me if I were still smoking. When I quit, I was smoking about a pack per day. So, in order to meet that threshold for me, a Daily would need to last an entire day from morning to bedtime, assuming I maintained a typical schedule of stepping outside roughly every other hour or so for 5-10 minutes.

For the sake of science, I've gone through 6 of them over the past week, and am still working on number seven. So far, they all have consistently lasted about 24 hours before giving up the ghost, give or take an hour or two.

Mind you, I'm not chain vaping the things, just using them in the same manner that I used to smoke--stepping outside every hour or hour and a half for 5 to 10 minutes during the 16-ish hours that I'm awake. The drags I took were about 2-4 seconds long, with about the same amount of suction that I used as a smoker, and I took one to three drags per minute.

If I tried to chain-vape a Daily, I doubt they'd last more than 3 hours (and I'd either have the mother of all nic buzzes or be puking my guts out).

They deliver. I'm impressed. They're a step up from the other disposables I've tried.

Price

MSRP for a Daily is \$5.99. For me, given my week-long pack-a-day simulation for this review, that puts the Daily on par with buying a pack a day. So, it's not cheap, but if you smoke a pack or less a day, it's competitive with buying cigarettes, yet still more expensive over the medium to long term than going straight to something like a basic eGo setup with decent clearomizers.

From a practical standpoint, the cigalikes I've tried before had a much worse bang-for-the-buck factor, costing anywhere from 1.5x to over twice what you'd spend on cigarettes and failing to come anywhere close to the stated longevity.

The Daily seems to be an okay middle ground as far as disposables go--not too expensive relative to a pack of cigarettes, and noticeably more reliable and consistent than the junky stuff.

Verdict

Smokers trying to quit through vaping tend to run into a number of pain points in the critical earliest days. At this point, they're usually trying to replace smoking with something that feels *like* smoking, and they're transitioning through not just a nicotine addiction, but also the physical/psychological aspect of the habit.

So, what they generally want is something that gives them the same feeling as smoking *without* being a gigantic pain in the ass or requiring a level of acclimatization that exceeds their threshold of frustration.

I think this is a good device for flipping smokers, especially those who choke on larger setups. My wife, for example, has tried several different devices and they all seem to make her cough or simply don't satisfy when dialed down. This device, she actually likes.

Electronic Patent Application Fee Transmittal				
Application Number:		14925968		
Filing Date:		28-Oct-2015		
Title of Invention:		NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF		
First Named Inventor/Applicant Name:		Adam BOWEN		
Filer:		Richard Douglas Shoop/Mary Buggie		
Attorney Docket Number:		13211-713.303		
Filed as Small Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Request for Prioritized Examination	2817	1	2000	2000
Pages:				
Claims:				
Miscellaneous-Filing:				
PROCESSING FEE, EXCEPT PROV. APPLS.	2830	1	70	70
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 1 month with \$0 paid	2251	1	100	100
Miscellaneous:				
Request for Continued Examination	2801	1	600	600
Total in USD (\$)				2770

Electronic Acknowledgement Receipt

EFS ID:	26695589
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Mary Buggie
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	19-AUG-2016
Filing Date:	28-OCT-2015
Time Stamp:	15:33:04
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	\$2770
RAM confirmation Number	1957
Deposit Account	504050
Authorized User	SHOOP, RICHARD D

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 CFR 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 CFR 1.17 (Patent application and reexamination processing fees)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_RCE_Track1_Ext_Response_Decl_Exhibits.pdf	3225135	yes	44
			1fd1f382fd81fa09f7706292bb4c37116159b7c8		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Request for Continued Examination (RCE)		1	1	
	TrackOne Request		2	2	
	Extension of Time		3	3	
	Amendment Submitted/Entered with Filing of CPA/RCE		4	4	
	Claims		5	8	
	Applicant Arguments/Remarks Made in an Amendment		9	18	
	Affidavit-traversing rejectns or objectns rule 132		19	44	
	Warnings:				
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	36104	no	2
			6689f4c2e5a25fe80b50cd5c128c89ce5e8a2a11		
Warnings:					
Information:					
Total Files Size (in bytes):			3261239		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 1 of 2

U. S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	666	US- 8,809,261	8/19/2014	Elschly et al.	
	669	US- 8,881,737	11/11/2014	Collett et al.	
	667	US- 2015/0038567	2/5/2015	Herkenroth et al.	
	580	US- 2016/0174611**	6/23/2016	Monsees et al.	
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			
		US-			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	668	EP2152313B1	9/3/2014	McNeil AB		

Examiner
SignatureDate
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT***(Use as many sheets as necessary)***Complete if Known**

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

Sheet 2 of 2

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	587	MONSEES et al.; U.S. Pat. Appl. # 15/165,954 entitled "Devices for vaporization of a substance," filed 5/26/2016	
	588	MONSEES et al.; U.S. Pat. Appl. # 15/166,001 entitled "Electronic vaporization device," filed 5/26/2016	
	589	MONSEES et al.; U.S. Pat. Appl. # 15/165,972 entitled "Portable devices for generating an inhalable vapor," filed 5/26/2016	
	665	BOWEN et al.; U.S. Pat Appl. # 15/101,303 entitled "Nicotine liquid formulations for aerosol devices and methods thereof," filed 6/2/2016	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.



(11) **EP 2 152 313 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention
of the grant of the patent:
03.09.2014 Bulletin 2014/36

(21) Application number: **08741851.3**

(22) Date of filing: **21.04.2008**

(51) Int Cl.:
A61K 47/18 (2006.01) **A24B 15/16** (2006.01)
A24B 15/30 (2006.01) **A61K 31/465** (2006.01)
A61K 9/08 (2006.01) **A61K 9/20** (2006.01)
A61K 9/48 (2006.01) **A61K 9/68** (2006.01)
A61P 25/34 (2006.01) **A23L 1/305** (2006.01)
A23G 3/44 (2006.01) **A23G 4/14** (2006.01)
A61K 9/00 (2006.01)

(86) International application number:
PCT/SE2008/000277

(87) International publication number:
WO 2008/140371 (20.11.2008 Gazette 2008/47)

(54) **ORAL NICOTINE FORMULATION BUFFERED WITH AMINO ACID**
MIT AMINOSÄURE GEPUFFERTE ORALE NIKOTIN-FORMULIERUNG
FORMULATION NICOTINIQUE ORALE TAMPONNÉE AUX ACIDES AMINÉS

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HR HU IE IS IT LI LT LU LV MC MT NL NO PL PT
RO SE SI SK TR

(30) Priority: **16.05.2007 SE 0701178**

(43) Date of publication of application:
17.02.2010 Bulletin 2010/07

(73) Proprietor: **McNeil AB**
25109 Helsingborg (SE)

(72) Inventors:
• **ANDERSSON, Sven-Börje**
SE-260 35 Odäkra (SE)
• **BERGENGREN, Gunnar**
SE-25223 Helsingborg (SE)
• **BOSSON, Bengt**
SE-256 55 Helsingborg (SE)
• **HUGERTH, Andreas**
SE-23733 Bjärred (SE)
• **NICKLASSON, Fredrik**
SE-23731 Bjärred (SE)
• **OLSSON, Roland**
SE-253 76 Helsingborg (SE)

(74) Representative: **Kirsch, Susan Edith**
Carpmaels & Ransford LLP
One Southampton Row
London WC1B 5HA (GB)

(56) References cited:
EP-A1- 1 304 048 **WO-A1-02/102357**
WO-A1-02/102357 **WO-A1-03/055486**
WO-A2-2005/023227

- **BECKETT A H ET AL:** "Buccal absorption of basic drugs and its application as an in vivo model of passive drug transfer through lipid membranes", **JOURNAL OF PHARMACY AND PHARMACOLOGY**, JOHN WILEY & SONS LTD, LONDON; GB, vol. 19, 1 December 1967 (1967-12-01), pages 31S-41S, XP009142973, ISSN: 0022-3573
- **OGAWA T. ET AL:** 'Screening of Bitterness-Suppressing Agents for Quinine: The Use of Molecularly Imprinted Polymers' **JOURNAL OF PHARMACEUTICAL SCIENCES** vol. 94, no. 2, February 2005, pages 353 - 362, XP009068797
- **OGAWA T. ET AL:** 'The Combination Effect of L-Arginine and NaCl on Bitterness Suppression of molecularly imprinted polymers' **CHEM. PHARM. BULL.** vol. 52, no. 2, 2004, pages 172 - 177, XP003023513

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Description**Technical Field**

5 [0001] This invention relates to nicotine-containing pharmaceutical formulations for intraoral delivery of nicotine to a subject. The formulations comprise one or more amino acids as buffering agents. Of specific interest are endogenous amino acids. Also contemplated are a method and a system for delivering nicotine as well as use and production of said formulations.

10 **Background of the invention**

[0002] Tobacco dependence and reduction thereof is a desirable goal. In recent years, with the recognition of the harmful effects of tobacco smoking, there have been numerous campaigns and programs by governmental agencies and various health groups and other interested organisations to disseminate information about the adverse health effects 15 resulting from tobacco smoking. Moreover, and as a result of this recognition of the harmful effects, there have been many programs directed to attempts in reducing smoking incidence.

[0003] Nicotine is an organic compound and is the principal alkaloid of tobacco. Nicotine is the chief addictive ingredient in the tobacco used in cigarettes, cigars, snuff and the like. Nicotine is also an addictive drug, and smokers characteristically display a strong tendency to relapse after having successfully stopped smoking for a time. Nicotine is the world's 20 second most used drug, after caffeine from coffee and tea.

[0004] The main problem with tobacco smoking is its enormous implications on health. It is estimated that smoking related diseases cause some 3 - 4 million deaths per year. According to Centers for Disease Control and Prevention, cigarette smoking among adults - United States, 1995. MMWR 1997; 46:1217 - 1220 around 500,000 persons in USA die each year as a result of tobacco use. In fact, excessive smoking is now recognised as one of the major health 25 problems throughout the world. This grim consequence of tobacco smoking has urged many medical associations and health authorities to take very strong actions against the use of tobacco.

[0005] Even though tobacco smoking is decreasing in many developed countries today it is hard to see how the societies could get rid of the world's second most used drug. The incidence of smoking is still rising in many countries, especially in less developed countries.

30 [0006] The most advantageous thing a heavy smoker can do is to stop smoking completely or at least to reduce his/her smoking. Experience shows, however, that most smokers find this extremely difficult since, mostly, tobacco smoking results in a dependence disorder or craving. The World Health Organization ("WHO") has in its International Classification of Disorders a diagnosis called Tobacco Dependence. Others like the American Psychiatric Association call the addiction Nicotine Dependence. It is generally accepted that these difficulties to stop smoking result from the fact that those heavy 35 smokers are dependent on nicotine. The most important risk factors related to health are, however, substances that are formed during the combustion of tobacco, such as carcinogenic tar products, carbon monoxide, N-nitrosamines, aldehydes, and hydrocyanic acid.

Effects of nicotine

40 [0007] Nicotine is an addictive poisonous alkaloid $C_5H_4NC_4H_7NCH_3$, derived from the tobacco plant. Nicotine is also used as an insecticide. The administration of nicotine (for example, in the form of smoking a cigarette, cigar or pipe) can give a pleasurable feeling to the smoker. However, smoking has health hazards and it is, therefore, desirable to formulate an alternative way of administering nicotine in a pleasurable and harmless manner that can be used to facilitate withdrawal 45 from smoking and/or used as a replacement for smoking.

[0008] When smoking a cigarette, nicotine is quickly absorbed into the smoker's blood and reaches the brain within around ten seconds after inhalation. The quick uptake of nicotine gives the consumer a rapid satisfaction, or kick. The satisfaction usually lasts during the smoking time of the cigarette and for a period of time thereafter. The poisonous, 50 toxic, carcinogenic, and addictive nature of smoking has provided strong motivation to develop methods, compositions and devices, which can be used to break the habit of smoking cigarettes.

Nicotine replacement products

55 [0009] One way to reduce smoking is to provide nicotine in a form or manner other than by smoking and some products have been developed to fulfil this need. Nicotine containing formulations are currently the dominating treatments for tobacco dependence.

[0010] The successes in achieving reduction in the incidence of smoking have been relatively poor using presently known products. The present state of the art involves both behavioural approaches and pharmacological approaches.

More than 80 % of the tobacco smokers who initially quit smoking after using some behavioural or pharmacological approach to singly reduce smoking incidence generally relapse and return to the habit of smoking at their former rate of smoking within about a one year's period of time.

[0011] As an aid for those who are willing to stop smoking there are several ways and forms of nicotine replacement products available on the market. Several methods and means have been described for diminishing the desire of a subject to use tobacco, which comprises the step of administering to the subject nicotine or a derivative thereof as described in e.g. U.S. Patent Number 5,810,018 (oral nicotine-containing spray), U.S. Patent Number 5,939,100 (nicotine-containing micro spheres) and U.S. Patent Number 4,967,773 (nicotine-containing lozenge).

[0012] Nicotine-containing nose drops have been reported (Russell et al., British Medical Journal, Vol. 286, p. 683 (1983); Jarvis et al., Brit. J. of Addiction, Vol. 82, p. 983 (1987)). Nose drops, however, are difficult to administer and are not convenient for use at work or in other public situations. Ways of administering nicotine by way of delivering directly into the nasal cavity by spraying is known from U.S. Patent Number 4,579,858, DE 32 41 437 and WO93/12764. There may be local nasal irritation, however, with use of nasal nicotine formulations. The difficulty in administration also results in unpredictability of the dose of nicotine administered.

[0013] The use of skin patches for transdermal administration of nicotine has been reported (Rose, in Pharmacologic Treatment of Tobacco Dependence, (1986) pp. 158-166, Harvard Univ. Press). Nicotine-containing skin patches that are in wide use today can cause local irritation and the absorption of nicotine is slow and affected by cutaneous blood flow.

[0014] Also, inhaling devices resembling a cigarette are known for uptake of nicotine vapours as suggested in U.S. Patent Number 5,167,242. Said means and methods address the problems associated with addiction to nicotine.

[0015] One successful product that is used as a smoking substitute and/or as a smoking cessation aid and which is based on nicotine, is the chewing gum Nicorette®. This product was one of the first nicotine replacement forms that was approved by the Food and Drug Administration (FDA) and is still one of the most used nicotine replacement products. Nicorette® chewing gum has been on the market in about 60 countries for several years. In this chewing gum the nicotine is present in the form of a complex with an insoluble cation-exchanger (polacrilix) that is dispersed in a gum base. The nicotine is slowly released from the gum due to chewing and will reach similar plasma levels as when smoking a cigarette after about 30 minutes depending on the chewing technique, i.e. slow or active. Patents related to this product are e.g. U.S. Patent Number 3,877,468, U.S. Patent Number 3,901,248 and U.S. Patent Number 3,845,217.

Prior art and problems thereof

[0016] WO 02/102357 discloses a coated nicotine-containing chewing gum. This gum provides improved transmucosal absorption of nicotine in the oral cavity. Thereby is achieved more of a cigarette-like sense of satisfaction and a more rapid reduction of the urge to smoke. Most buffers proposed in WO 02/102357 possess off-notes, however, and one or more flavouring agents need be added to the gum in order to cover the off note taste. Certain salts of glycine are mentioned in a list of buffers without any mentioning of whether these salts have any disagreeable taste or not.

[0017] WO 2005/023227 discloses nicotine-containing compositions wherein nicotine is absorbed into and/or onto cellulose of non-seed organism origin, especially from algae, bacteria and/or fungi. As with WO 02/102357 also most buffers proposed in WO 2005/023227 possess off-notes. Certain salts of glycine are mentioned in a list of buffers without any mentioning of whether these salts have any disagreeable taste or not.

[0018] Oqawa Tazuko et al.: "Screening of bitterness-suppressing agents for quinine: The use of molecularly imprinted polymers"; Journal of Pharmaceutical Sciences, Vol. 94, No. 2 (Feb 2005), 353 -362, assumes that a few amino acids may suppress the bitterness of quinine, while most amino acids do not suppress such bitterness. Anyhow, Oqawa et al do not disclose any utility for amino acids as buffering agents in nicotine-containing formulations. Quinine and nicotine are chemically and pharmacologically very different, which means that teachings on quinine cannot as such be applied on nicotine.

[0019] WO 03/055486 seeks to provide formulations with fast satisfaction of nicotine craving without smoking.

[0020] Problems with off-notes from buffers may arise with all other nicotine-containing pharmaceutical formulations for oral delivery, such as mouth sprays, chewable tablets, tablets, lozenges, chewing gums, capsules, lipid-filled micro gels, oral films, and different candy-type formulations.

[0021] Thus, there is a need to ameliorate nicotine-containing pharmaceutical formulations for oral delivery in order to avoid off-notes from the buffers used. Many of the buffering compounds disclosed as novel and inventive in the present application are especially useful as they are endogenous amino acids, i.e. they are already present in the human body.

[0022] To date nothing has been disclosed on the utility of amino acids as buffers in nicotine-containing pharmaceutical formulations. US 5,733,572 discloses gas filled micro-spheres, which, as stated in a long and non-substantiated laundry list, may further comprise nicotine and certain amino acids, the latter though not for buffering purposes, but for achieving a depot action effect.

Summary of the Invention

[0023] When formulating a medical product intended to dissolve in the oral cavity the organoleptic characteristics are essential. Besides, in many cases there is a need to obtain optimal pH in the oral cavity to be able to achieve sufficiently rapid uptake of the active ingredient. By using a buffering agent in the product said pH can be adjusted. However, the number of pharmaceutically appropriate buffering agents is limited and some of the most commonly used buffering agents possess distinct off-notes. Therefore, one or more flavoring agents are usually added to the formulation to cover these off-notes. Moreover, flavoring agents are also used in the formulation to accomplish a product with pleasant taste. The possibility of using a buffering agent with no or comparatively mild off-taste, facilitates the formulation work and reduces the complexity of the flavoring process. Many of the amino acid type of buffering agents possess no unpleasant intrinsic taste and consequently, the use of such excipients in nicotine-containing products for oral uptake has been found to be beneficial by the present inventors.

[0024] Another important criterion when choosing buffering agents in nicotine-containing formulations is the toxicity. Many of the common amino acids can be classified as harmless since they are present in large amounts, several grams per day, in common nutrition.

[0025] Other advantages in using amino acids as buffers in nicotine-containing formulations encompass lack of unpleasant smell and that many of the amino acids of interest have monographs in both USP/NF and Ph.Eur and that many of them are found in the FDA-list of inactive ingredients.

[0026] In view of the foregoing disadvantages known in the art when trying to deliver nicotine to a subject so as to obtain a transmucosal uptake of nicotine in the oral cavity of the subject the present invention provides a new and improved product, systems and methods for obtaining a transmucosal uptake of nicotine in the oral cavity of the subject, while avoiding off-notes from the buffer used.

[0027] An object of the present invention is to provide an efficient and effective product, as well as methods and systems for uptake of nicotine in a subject and to avoid the disadvantages of such previously known products and methods.

[0028] The present invention provides for an oral formulation according to claim 1 comprising nicotine in any form, which is buffered with at least one amino acid and which comprises a pH-adjusting compound should the pH-adjusting capacity of said at least one amino acid be insufficient.

[0029] Also described is a method for delivering nicotine in any form to a subject comprising administering to a subject an oral formulation comprising nicotine in any form into the oral cavity of the subject and if needed allowing the nicotine in any form in the oral formulation to be released in the saliva in the oral cavity and absorbed into the systemic circulation of the subject as well as a method for producing said oral formulation. In a mouth spray the nicotine is directly available wherefore it need not be released as such in the saliva as said above. Hence the phrase "if needed" is inserted in the preceding sentence and in corresponding sentences below and in the claims.

[0030] The present invention further provides a use of the oral formulation described herein for obtaining reduction of the urge to smoke or use tobacco containing material and/or for providing a sense of smoking satisfaction without smoking, by the steps of replacing at least partly the tobacco containing material with the above said oral formulation, administering to a subject an oral formulation containing nicotine in any form into the oral cavity of the subject and if needed allowing the nicotine in any form of the oral formulation to be released in the saliva in the oral cavity and absorbed by the subject.

[0031] Furthermore, the present invention provides a system for delivering nicotine in any form to a subject, comprising said oral formulation and at least one other means for obtaining reduction of the urge to smoke or use of tobacco as well as a system for obtaining reduction of the urge to smoke or otherwise use tobacco and/or for providing a sense of smoking satisfaction without smoking, comprising an oral formulation as described above and at least one other method for obtaining reduction of the urge to smoke or otherwise use tobacco. Said system may be a system wherein the at least one other method is selected from the group consisting of administration through mouth sprays, nasal sprays, transdermal patches, inhaling devices, lozenges, tablets and parenteral methods, subcutaneous methods, and transmucosal methods; or other use of tobacco.

[0032] By using an amino acid as the only buffer, or as the main buffer, in said oral formulation the aforesaid problem with off-notes from the buffers used is solved. Further, such a buffer can, as said supra, be regarded as adequate from a toxicity point of view.

Detailed Description of the Invention*Definitions*

[0033] As used herein, the term "oral formulation" or similar intends to mean all formulations being suitable to be placed in the oral cavity for delivering nicotine essentially to the mucous membrane of the oral cavity.

[0034] The term "intraoral delivery" is herein intended to mean delivery into the systemic blood circulation by means

of absorption of an active principle by any tissue of the oral cavity.

[0035] The term "complete reduction" or "complete" is herein intended to mean complete or substantially complete reduction.

5 [0036] The term "controlled release" is intended to mean a release of nicotine from an oral formulation in the oral cavity of the subject, whereby active sucking or other manipulation of the oral formulation is controlling the amount of nicotine released.

[0037] The term "slow release" is intended to mean that nicotine is released from the oral formulation upon sucking or other manipulation over a period of time for example, several minutes to an hour.

[0038] The term "unit formula" is intended to mean one oral formulation unit.

10 [0039] The term "transient" is intended to mean a non-permanent change, upon which the relevant state, e.g. biological or physiological state, after a certain period of time will return to its value or behaviour prior to said change.

[0040] The terms "buccal" and "buccally" are herein intended to pertain to all of or any part of the tissue of the oral cavity.

Useful oral formulations

15 [0041] Most dosage forms intended for oral delivery of nicotine benefit from using selected amino acids as the only or main buffering agent. These formulations include e.g. mouth sprays, chewing gums, tablets, melt tablets, lozenges, hard boiled candies, chewy candies, gummies, capsules, oral films, and liquid as well as powder formulations for intraoral and pulmonary inhalation.

20 [0042] Particular formulations are mouth sprays. These are discreet dosage forms being useful for obtaining a rapid uptake of nicotine through the mucosa of the oral cavity. Mouth sprays may be sprayed straight into the oral cavity or alternatively under the tongue. Below Example 3 discloses the manufacturing of a mouth spray according to the invention.

[0043] The amount of gum base in a chewing gum according to the invention is about 15 - 80 % by weight of the total gum core, and preferably about 40-80%. The amount of gum base employed for slow release of nicotine is usually in the higher ranges when nicotine is employed *per se* or when an absorbed form is used.

25 [0044] The gum base may be of any conventional nature known in the art. For example, it may comprise a gum base of natural or synthetic origin readily available from a commercial source. Natural gum bases include e.g. chicle, jelutong-, lechi de caspi-, soh-, siak-, katiau-, sorwa-, balata-, pendere-, malaya-, and peach gums, natural caoutchouc and natural resins such as cammar and mastix. Synthetic gum bases are a mixture of:

- 30
- elastomers (for example polymers and/or masticating substances),
 - plasticizers (for example resins, elastomers and/or solvents)
 - fillers (for example texturizers and/or water-insoluble adjuvants),
 - softeners (for example fats),
 - 35 - emulsifiers,
 - waxes,
 - antioxidants,
 - and anti-tacking agents (for example vinyl polymers and/or hydrophilic resins)

40 [0045] Other examples of gum bases are gums including agar, alginate, arabic gum, carob gum, carrageenan, ghatti gum, guar gum, karaya gum, pectin, tragacanth gum, locust bean gum, gellan gum and xanthan gum.

[0046] Examples of gelling agents comprise gum arabic, starch, gelatine, agar, and pectin.

45 [0047] When the nicotine in any form and the buffering agent or agents are incorporated in the chewing gum mass in accordance with the present invention, it is possible to employ a wide variety of chewing gum compositions and amounts of the chewing gum base.

[0048] Different chewing gum products may be composed depending on the consumers' preference and the purpose of use, in respect of the nicotine level, nicotine distribution and other additives.

50 [0049] Further below follow Examples on useful chewing gums, tablets, melt tablets, mouth sprays, soft capsules, hard boiled candies, oral films, gummies and chewy candies according to the present invention. On the basis of said Examples also other useful embodiments are envisageable.

The buffering agent

55 [0050] Absorption of nicotine from the oral cavity to the systemic circulation is dependent on the pH of the saliva, pH of the blood plasma and the acid-base equilibrium of nicotine, which is about $pK_a \approx 7.8$ at 37°C . Assuming a pH of the saliva of 6.8, only about 10% of the nicotine will be in the non-charged base form. Thus, in order to promote absorption of nicotine in a free base form, which is the form predominantly absorbed through the mucosa, the pH of the saliva must be increased. At a pH of 9.0 more than 90% of the nicotine will be in the free readily absorbable base form.

[0051] According to the invention, the oral formulation is buffered by use of substances, agents or other means, which at least partly comprise an amino acid, preferably an endogenous amino acid, and/or a salt thereof.

[0052] As said above many of the amino acid type of buffering agents possess no unpleasant intrinsic taste. Further, many of the common amino acids, especially the endogenous ones, can be classified as harmless from a toxicity point of view since they are present in large amounts, several grams per day, in common nutrition.

[0053] As least some of the below criteria should preferably be used when selecting amino acids useful as buffers in nicotine-containing formulations:

- 1) pKa in the interval 8,0 - 9,6 (as the system should buffer in the pH area above nicotine's pKa value at 25°C).
- 2) Solubility in water more than around 10 g/kg.
- 3) Useful from a toxicity point of view.
- 4) Preferably already used as buffer in pharmaceutical formulations devoid of nicotine.

[0054] The most useful amino acids are listed in below Table 1.

Table 1 Especially useful amino acids.

Compound	CAS Number	pKa value (in interval 8 - 9,6)	Solubility in Water, g/kg
Arginine	74-79-3	9,00	182,6 ^{a)}
Asparagine	70-47-3	8,73	25,1
Glutamic acid	56-86-0	9,58	8,61 ^{a)b)}
Glutamine	56-85-9	9,00	42
Glycine*	56-40-6	9,58	250,9
Histidine	71-00-1	9,09	43,5
Isoleucine	73-32-5	9,60	34,2
Leucine	61-90-5	9,58	22,0
Lysine	56-97-1	9,16	Very soluble ^{a)b)}
Methionine	63-68-3	9,08	56
Phenylalanine	63-91-2	9,09	27,9
Serine	56-45-1	9,05	50,2
Threonine	72-19-5	8,96	98,1
Valine	72-18-4	9,52	88,5
Cysteic acid	13100-82-8	8,70	Very soluble
N-Glycylglycine	556-50-3	8,10	No information
Ornithine	70-26-8	8,76	Very soluble
* = Comparative			
a) reported as buffer in non-nicotine-containing pharmaceutical formulations.			
b) low or uncertain value on solubility in water.			

[0055] The captioned data on the amino acids are taken from "Handbook of Chemistry and Physics", 85th edition; Table 7-1 ("20 standard amino acids that are the basic constituents of proteins") and Table 7-2 ("Amino acids and related compounds of biochemical importance").

[0056] The buffering is designed so as to achieve a transient buffering of the saliva of a subject at an elevated pH value during melting, disintegration or dissolution of the oral formulation. As the change is transient, the pH will return to its normal value after a certain period of time.

[0057] By employing said change, here an increase, in said pH of the saliva the transmucousal uptake of nicotine in the oral cavity is changed, e.g. increased compared to the nicotine uptake when the saliva is not buffered according to the invention. Also, since the transmucousal uptake of nicotine in the oral cavity according to the invention is faster than for nicotine not being buffered according to the invention, less nicotine will be swallowed to reach the gastrointestinal (G.I.) tract. The nicotine that reaches the G.I. tract will be subjected to first pass metabolism, which reduces the total

amount of intact nicotine absorbed. This means that the bioavailability of nicotine that is not co-administered with a buffer will generally be lower than when administered together with a buffer.

[0058] Further embodiments of the invention includes oral dosage forms being buffered with an amino acid in combination with other buffers or pH-adjusting compounds, preferably selected from the group consisting of a carbonate including bicarbonate or sesquicarbonate, phosphate, glycerophosphate or citrate of an alkali metal, such as potassium or sodium, or ammonium, and mixtures thereof.

[0059] Still further embodiments may encompass use of an amino acid together with different phosphate systems, such as trisodium phosphate, disodium hydrogen phosphate, and tripotassium phosphate, dipotassium hydrogen phosphate, and calcium hydroxide, sodium glycinate, trometamol and mixtures thereof.

[0060] Alkali metal carbonates and phosphates are preferred additional buffering agents or pH-adjusting compounds.

[0061] In order to increase the buffering capacity still further without correspondingly increasing the pH, one may in specific embodiments use a second or auxiliary buffering agent to the first buffering agent, such as e.g. sodium or potassium bicarbonate buffers. In addition a strong base, e.g. sodium hydroxide, may be added to the formulation in order to raise its basic property. Thereby should be strived to maintain a pleasant taste. The second or auxiliary buffering agent may be selected from the group consisting of alkali metal bicarbonates that are preferred for this purpose. Thus, further embodiments of the invention may comprise an amino acid and a mixture of an alkali metal carbonate or phosphate and alkali metal bicarbonate. Some useful mixture ratios are provided in the below Examples.

[0062] The amount of the buffering agent and optional pH-adjusting compounds in the oral formulation is preferably sufficient in the specific embodiments to transiently maintain the pH of the saliva in the oral cavity above 7, e.g. pH 7 - 10.

[0063] The nicotine may be administered in different forms, e.g. in different complexes or salts. The amount of buffer and optional pH-adjusting compounds required to achieve an increase in pH of the different administered nicotine forms is readily calculated by the skilled man in the art. The extent and duration of the increase in pH is dependent on type and amount of the buffering agent(s) used as well as where is further described within the paragraphs below.

The active ingredient

[0064] According to the invention, the present oral formulation comprises nicotine in any form (for example free base, salt or complex).

[0065] With nicotine it is intended to include nicotine, 3-(1-methyl-2-pyrrolidinyl)-pyridine, with its base form, including synthetic nicotine as well as nicotine extracts from tobacco plants, or parts thereof, such as the genus *Nicotiana* alone or in combination; or pharmaceutically acceptable salts.

[0066] The nicotine compound should be in a saliva soluble form or facilitate a rapid release of the nicotine into the saliva in the oral cavity and, further, the subsequent uptake of the nicotine from the saliva in the oral cavity into the systemic circulation of the subject. When the nicotine prevails in the form of nicotine resin complex, NRC, its release of nicotine is modified in the presence of a buffer.

[0067] In preferred embodiments, the nicotine in any form is selected from the group consisting of the free base form of nicotine, a nicotine salt, a nicotine derivative, such as a nicotine cation exchanger, a nicotine inclusion complex or nicotine in any non-covalent binding, nicotine bound to zeolites, nicotine bound to cellulose or starch micro spheres, and mixtures thereof.

[0068] Numerous nicotine salts are known, and may be used, e.g. the salts presented in Table 2, preferably monotartrate, hydrogen tartrate (also called bitartrate or bitartrate dihydrate), citrate, malate, and/or hydrochloride.

Table 2 Possible acids used for nicotine salt formation

Acid	Molar ratio* of acid:nicotine
Formic	2:1
Acetic	3:1
Propionic	3:1
Butyric	3:1
2-Methylbutyric	3:1
3-Methylbutyric	3:1
Valeric	3:1
Lauric	3:1
Palmitic	3:1
Tartaric	2:1
Citric	2:1
Malic	2:1

(continued)

	Acid	Molar ratio* of acid:nicotine
5	Oxalic	2:1
	Benzoic	1:1
	Gentisic	1:1
	Gallic	1:1
	Phenylacetic	3:1
10	Salicylic	1:1
	Phthalic	1:1
	Picric	2:1
	Sulfosalicylic	1:1
	Tannic	1:5
15	Pectic	1:3
	Alginic	1:2
	Hydrochloric	2:1
	Chloroplatinic	1:1
20	Silicotungstic	1:1
	Pyruvic	2:1
	Glutamic	1:1
	Aspartic	1:1
25	* recommended at the time of production	

[0069] The inclusion complex may be a nicotine-cyclodextrin (1-1) compound, such as nicotine- β -cyclodextrin.

[0070] Suitable cation exchangers are given in below Table 3 and are further disclosed in U.S. Patent Number 3,845,217. Preferred are nicotine cation exchangers of polyacrylates, such as the Amberlite collection from Rohm & Haas.

Table 3 Representative cation exchangers

	Name	Type of crosslinked polymer	Manufacturer
	Amberlite IRC 50	Divinylbenzene-methacrylic acid	Rohm & Haas
35	Amberlite IRP 64	Divinylbenzene-methacrylic acid	Rohm & Haas
	Amberlite IRP 64M	Divinylbenzene-methacrylic acid	Rohm & Haas
	BIO-REX 70	Divinylbenzene-acrylic acid	BIO-RAD Lab.
	Amberlite IR 118	Styrene-divinylbenzene	Rohm & Haas
	Amberlite IRP 69	Styrene-divinylbenzene	Rohm & Haas
40	Amberlite IRP 69M	Styrene-divinylbenzene	Rohm & Haas
	BIO-REX 40	Phenolic	BIO-RAD Lab.
	Amberlite IR 120	Styrene-divinylbenzene	Rohm & Haas
	Dowex 50	Styrene-divinylbenzene	Dow Chemical
	Dowex 50W	Styrene-divinylbenzene	Dow Chemical
45	Duolite C 25	Styrene-divinylbenzene	Chemical Process Co
	Lewatit S 100	Styrene-divinylbenzene	Farbenfabriken Bayer
	Ionac C 240	Styrene-divinylbenzene	Ionac Chem.
	Wofatit KP S 200	Styrene-divinylbenzene	I.G. Farben Wolfen
50	Amberlyst 15	Styrene-divinylbenzene	Rohm & Haas
	Duolite C-3	Phenolic	Chemical Process
	Duolite C-10	Phenolic	Chemical Process
	Lewatit KS	Phenolic	Farbenfabriken Bayer
	Zerolit 215	Phenolic	The Permutit Co.
55	Duolite ES-62	Styrene-divinylbenzene	Chemical Process
	BIO-REX 63	Styrene-divinylbenzene	BIO-RAD Lab.
	Duolite ES-63	Styrene-divinylbenzene	Chemical Process

(continued)

Name	Type of crosslinked polymer	Manufacturer
Duolite ES-65	Phenolic	Chemical Process
Ohelex 100	Styrene-divinylbenzene	BIO-RAD Lab.
Dow Chelating Resin A-1	Styrene-divinylbenzene	Dow Chemical Company
CM Sephadex C-25	Dextran	Pharmacia Fine Chemicals
SE Sephadex C-25	Dextran	Pharmacia Fine Chemicals

[0071] One or more additives may be added to the present oral formulation. Additives are further described in the below paragraph *Other additives to the oral formulation*.

Amount and distribution of the nicotine in the oral formulation

[0072] The nicotine in any form according to the invention is formulated to provide the subject with a dose to achieve an effect. The effect may be to provide a sense of smoking satisfaction without smoking. Another effect of the administered nicotine in any form may be a reduction of the urge to smoke or use tobacco.

[0073] The effect may also be a combination of reduction of said urge and providing a sense of smoking satisfaction without smoking. The amount of the nicotine should be sufficient to provide such an effect in a subject. This amount may, of course, vary from person to person.

[0074] According to the invention, embodiments of the oral formulation comprise embodiments wherein nicotine in any form is present in an amount of 0.05 - 8 mg calculated as the free base form of nicotine per unit dose of the oral formulation. This may in different embodiments include 0.1, 0.5, 1, 2, 3, 4, 5, 6 or 8 mg calculated as the free base form of nicotine per unit dose.

[0075] Still preferred embodiments may contain embodiments where the nicotine in any form is present in an amount of 0.5 - 6 mg calculated as the free base form of nicotine per unit dose of the oral formulation.

[0076] Even more preferred embodiments contain the nicotine in any form in an amount of 0.5 - 5 mg calculated as the free base form of nicotine per unit dose of the oral formulation.

[0077] The nicotine in any form may be distributed in the oral formulations in different embodiments. Different distributions of the nicotine throughout the oral formulations will imply administration of the nicotine to the subject in different ways. This may, then, provide several possibilities to adjust the composition of the oral formulation according to different needs of different subjects depending on the urge to smoke or use tobacco of the subject. In the below Examples are disclosed different such embodiments.

Other additives to the oral formulation

[0078] A strong base, e.g. sodium hydroxide, may be added to the formulation in order to give it a weak basic property.

[0079] Other additives may be added optionally to the oral formulation. Optional additives comprise at least one or more additives selected from the group consisting of solvents, such as ethanol and water; co-solvents, such as propylene glycol; stabilisers, such as preservatives, e.g. antioxidants; softeners, such as sorbitol and glycerine; thickening agents, such as colloidal silicon dioxide; binding agents, such as xanthan gum; filling agents, such as mannitol, isomalt, cocoa powder and Croscopovidone; solubilizers, such as Polysorbate 80 and Atmos 300; rubbers, lipid barriers, such as sucrose fatty acid esters and hydrogenated vegetable oils; film forming agents, such as porcine gelatine, Pullulan, carrageenan, pectin, locust bean gum and xanthan gum; emulsifiers, such as pectin, soy lecithin, glycerol monostearate, castor oil and poloxamer; glidants, such as colloidal silicon dioxide; lubricants, such as magnesium stearate; coating agents, such as castor oil and sorbitol; melting vehicles, such as vegetable oils; sweeteners, flavours, aromatics, cooling agents, enhancers, colouring agents, vitamins, minerals, fluorine, breath fresheners, tooth whitening agents and mixtures thereof. According to the invention, at least one of such additives is optionally added to the product.

[0080] Enhancers may be added essentially to increase the transmucosal uptake of nicotine from the oral cavity.

[0081] Sweeteners are added essentially to improve the taste. Sweeteners comprise one or more synthetic or natural sugars, i.e. any form of carbohydrates suitable for use as sweetener, as well as so called artificial sweeteners such as saccharin, sodium saccharin, aspartame, e.g. NutraSweet®, acesulfame or Acesulfame K, potassium acesulfame, thau-matin, glycyrrhizin, sucralose, dihydrochalcone, alitame, miraculin, monellin, stevioside and neotame.

[0082] Suitable sweeteners may be selected from the group consisting of sugar alcohols, such as sorbitol, xylitol, single sugars including sugars extracted from sugar cane and sugar beet (sucrose), dextrose (also called glucose), fructose (also called levulose), and lactose (also called milk sugar); sorbitol, mannitol, glycerol, xylitol, erythritol, maltitol syrup (or hydrogenated starch hydrolyzate), isomalt, lactitol, and mixtures of sugars including glucose syrup, e.g. starch

hydrolysates, containing a mixture of dextrose, maltose and a range of complex sugars, invert sugar syrup, e.g. sucrose inverted by invertase (also called sucrase or sacchrase) containing a mixture of dextrose and fructose, high sugar content syrups such as treacle and honey containing a mixture of particular leavulose, dextrose, maltose, lactitole, sucrose, resins, dextrin and higher sugars; and malt or malt extracts.

[0083] The flavour and aroma additives may comprise one or more synthetic or natural taste-masking, flavouring or aromatizing agents. Flavour and aroma agents may be selected from essential oils including distillations, solvent extractions, or cold expressions of chopped flowers, leaves, peel or pulped whole fruit comprising mixtures of alcohols, esters, aldehydes and lactones; essences including either diluted solutions of essential oils, or mixtures of synthetic chemicals blended to match the natural flavour of the fruit, e.g. strawberry, raspberry and black currant; artificial and natural flavours of brews and liquors, e.g. cognac, whisky, rum, gin, sherry, port, and wine; coffee, tea, cocoa, and mint; fruit juices including expelled juice from washed, scrubbed fruits such as lemon, orange, and lime; spear mint, pepper mint, wintergreen, cinnamon, cacao/cocoa, vanilla, liquorice, menthol, eucalyptus, aniseeds, nuts (e.g. peanuts, coconuts, hazelnuts, chestnuts, wainuts, colanuts), almonds, raisins; and powder, flour, or vegetable material parts and ginger.

[0084] Colouring additives may be selected from dyes being approved as a food additive.

[0085] Stabilizing additives may be selected from the group consisting of antioxidants including vitamin E, i.e. tocopherole, ascorbic acid, sodium pyrosulfite, butylhydroxytoluene, butylated hydroxyanisole, edetic acid and edetate salts; and preservatives including citric acid, tartaric acid, lactic acid, malic acid, acetic acid, benzoic acid, and sorbic acid. Preferred embodiments comprise an antioxidant as the stabiliser, and even more preferably the antioxidant vitamin E and/or butylated hydroxytoluene (BHT).

Method for delivering nicotine in any form to a subject

[0086] The invention may be used to deliver nicotine to the subject (person) in a variety of ways. Described herein is a method for delivering nicotine in any form to a subject comprises the steps of:

- a) administering to a subject an oral formulation containing nicotine in any form according to the invention into the oral cavity of the subject, and
- b) if needed allowing the nicotine in any form in the oral formulation to be released in the saliva in the oral cavity and absorbed into the blood plasma of the subject. The method for delivering nicotine in any form may further comprise the steps of:
- c) administering the nicotine in any form in a sustained way over a period of time to the subject. Such a time period may be at least 5, 10, 20, 30 or 40 minutes.

Method for obtaining reduction of the urge to smoke or use of tobacco

[0087] Another feature of the invention is the ability to use the invention to reduce the urge to smoke. A use for obtaining reduction of the urge to smoke or use nicotine-containing tobacco products and/or for providing a sense of smoking satisfaction without smoking according to the invention comprises the steps of:

- a) replacing at least partly the nicotine-containing tobacco product with an oral nicotine-containing formulation devoid of tobacco,
- b) administering to a subject an oral formulation containing nicotine in any form into the oral cavity of the subject, and
- c) if needed allowing the nicotine in any form in the oral formulation to be released in the saliva in the oral cavity and absorbed by the subject.

[0088] In another embodiment, the use according to the invention further comprises the steps of administering the nicotine in any form in a sustained way over a period of time to the subject. The period of time may be at least 5, 10, 20, 30 or 40 minutes.

[0089] Further embodiments of the use for delivering nicotine to a subject may comprise the steps of combining administration of the oral formulation with at least one other method for obtaining reduction of the urge to smoke or use of tobacco.

[0090] Tobacco containing material may be material used for e.g. smoking, snuffing or chewing and may comprise a cigarette, a cigar, pipe tobacco, snuff, snus and chewing tobacco.

Sustained reduction of the urge to smoke or use of tobacco

[0091] The invention may also be used to reduce the urge to smoke or use tobacco. Still, to continue the feeling or sense of satisfaction of the subject, and to avoid that the craving returns, a sustained craving relief may be obtained

after the initial craving relief. A sustained craving relief is obtained by using the oral formulation in such a way as to allow a sustained uptake of the nicotine. The sustained craving relief and/or feeling or sense of satisfaction of the subject will continue as long as the subject maintains the blood plasma levels of nicotine at a level high enough to reach this sense of feeling.

- 5 **[0092]** The subject may achieve this by using the oral formulation over a period of time, such as 5, 10, 20, 30 or 40 minutes or longer, e.g. a slow release of the nicotine caused by a controlled release, e.g. by individual use.

Cessation of the urge to smoke or use of tobacco

- 10 **[0093]** For some of the users, it may be a goal to terminate the usage of nicotine completely, due to several reasons e.g. health, economical, social or behavioural. This cessation of smoking or the urge to use tobacco may be achieved by further decreasing the amount of nicotine in any form gradually over time. In a specific embodiment of the invention, the method described above for obtaining craving relief may further comprise the steps of decreasing the amount of nicotine in the oral formulation described above gradually over time, so as to achieve a complete relief of tobacco craving.

15 This method results in a weaning process gradually over time.

[0094] Different types of smokers reach the sense of reduced craving at different plasma levels of nicotine. This may, of course, affect the individual types of administration programs of an oral formulation according to the invention. Different types of smokers include e.g. peak seekers or smokers that crave for a plasma level of nicotine constantly being above the level for withdrawal symptoms.

- 20 **[0095]** One strategy may be to lower the frequency of the administered oral formulation. Other embodiments include varying the dose of the nicotine in said oral formulations as well as the combination of these two. Also, the strategy may include an oral formulation with substantially no nicotine in any form. Such an oral formulation may be administered at the end of the treatment period, when the craving is low or substantially absent.

25 *Systems for delivering nicotine and for obtaining craving relief*

[0096] According to the invention there is a system according to the claims for delivering nicotine in any form to a subject particularly for obtaining craving relief. Such a system comprises an oral formulation according to the invention and at least one other means for obtaining reduction of the urge to smoke.

- 30 **[0097]** Another system according to the invention may also be a system for obtaining reduction of the urge to smoke or use of tobacco and/or for providing a sense of smoking satisfaction without smoking. Such a system comprises an oral formulation according to the invention and at least one other method or means for obtaining reduction of the urge to smoke or use tobacco. Other methods and means may also be a concomitant or concurrent method selected from the group consisting of administration through mouth sprays, nasal sprays, transdermal patches, inhaling devices, lozenges, tablets and parenteral methods, subcutaneous methods, and transmucousal methods; or use of tobacco.

35 **[0098]** In a specific embodiment, the at least one other method comprises administration of nicotine.

Use of the oral formulation

- 40 **[0099]** The use of the oral formulation according to the invention may include obtaining a fast and/or sustained and/or complete reduction of the urge to smoke and use tobacco or for providing a sense of smoking without smoking as described above.

[0100] The dose of the nicotine is chosen to give the subject an individual sensory perception and satisfaction with an effect of the nicotine in any form. The use of an oral formulation may also be a sole use according to the invention or a combination with other means or methods known in the field of drug abuse. Specifically, the present invention may be used in combination with other means as described above in the methods in the paragraphs above.

- 45 **[0101]** The use may give a quick reduction of the urge to smoke or use tobacco. Other embodiments include providing a slow reduction of the urge to smoke or use tobacco.

50 *Use for therapy and treatment*

[0102] The oral formulation according to the invention may be used in therapy and treatment. Said therapy may be a treatment of a disease selected from the group consisting of tobacco or nicotine dependence, Alzheimer's disease, Crohn's disease, Parkinson's disease, Tourette's syndrome, ulcerous colitis and post-smoking-cessation weight control.

- 55 **[0103]** Nicotine may also be used for an oral formulation according to the invention for the treatment of said diseases.

[0104] Further, nicotine may be used in the production of a nicotine-containing oral formulation according to the invention for the treatment of said diseases.

Production of the oral formulation

[0105] The oral formulations according to the present invention are basically produced according to methods known in the art. Exemplary, but not limiting, production methods are provided below under Examples.

[0106] In the below Examples is described mixing, rolling and scoring of chewing gums as well as compression of chewing gums. The below Examples also provide information on manufacturing of other embodiments of the present invention.

[0107] Conveniently, the compositions of additives according to the invention, e.g. the buffer system, are made simultaneously, according to known procedures in the art for formulating e.g. the buffers. Depending on the physical properties of the buffer system incorporated, it may be convenient to add the buffer system/s either with the liquid part or with the solid part of the composition. In the case of buffering systems available as fine powders, it may, of course, be most convenient to add those powders with the solid, powdered part of other additives. The final product may then be analysed and wrapped.

Analysis of nicotine

[0108] The analysis of nicotine uptake and effect according to the invention may be done according to standard procedures known in the art, e.g. using bioanalysis for the determination of nicotine or its metabolites in the plasma of a subject.

Examples

[0109] The below examples on embodiments of the present invention are illustrative and non-limiting. The skilled person may on the basis of the following examples envisage also other embodiments of the present invention. Batch sizes for the manufacture of the below formulations may be modified according to the actual need and to the actual production facilities. If not stated otherwise procedures and equipment known in the art are used in the below manufacturing.

[0110] In the below Examples the amino acids used are L-Arginine, Glycine and N-glycylglycine. The skilled person may though exchange L-Arginine, Glycine and N-glycylglycine for one or more other amino acids, such as amino acids selected from above Table 1, thereby adapting the amount(s) of amino acid according to state of the art methods. Further, the skilled person may readily calculate whether a pH-adjusting compound need be added. Accordingly in some of the below Examples a pH-adjusting compound has been added in addition to the buffer.

Example 1 Tablets

275 mg tablet with 2 mg nicotine

[0111]

Ingredients	Amount in composition (mg)
Nicotine bitartrate dehydrate	6,1
L-Arginine	17,9
Mannitol	210,9
Xanthan gum	11,0
Crospovidone	11,0
Flavoring agents	9,9
Aspartame	1,6
Acesulfame K	1,1
Magnesium stearate	5,5

Manufacturing process:

[0112] The above ingredients are blended. The blend is then compressed into tablets by means of direct compression

according to methods known in the art.

Example 2 Melt tablets

5 [0113] This is a tablet intended for melting in the mouth whereupon the melted material adheres to the oral mucosa where the nicotine is deposited for entering into the tissue.

400 mg melt tablet with 2 mg nicotine

10 [0114]

Ingredients	Relative amount in composition (%w/w)
Nicotine bitartrate dehydrate	1.5
15 Cocoa powder	35.0
Vegetable oil	41.6
L-Arginine	4.5
20 Mannitol	10.4
Titanium dioxide	2.7
Soy lecithin	1.0
Aspartame	0.4
25 Acesulfame K	0.2
Flavoring agents	2.7

Manufacturing process:

30

[0115] The manufacturing as such takes place at room temperature. A part of the fatty component, i.e. the vegetable oil, is melted. The solid components, i.e. the nicotine salt, the cocoa powder, the buffering agent, the mannitol, the titanium oxide, the sweeteners and the flavoring agents are added and mixed. A reduction of particle size of the solid components is performed by milling the mixture in a roll-refiner. If the solid components have already got the required particle size, e.g. by milling before the mixing with the fatty component, roll refining is dispensed with. After possible treatment in the roll-refiner the mixture is mixed with the rest of the melted vegetable oil or remelted (if solidified) and mixed with the rest of the melted vegetable oil. A mixing of the melt is performed in a suitable mixer. The liquid component, i.e. the soy lecithin, is added.

40 [0116] Tablets are subsequently made using suitable techniques, such as molding, extrusion or congealing, including pastillation, when necessary after suitable preconditioning. Also other suitable manufacturing methods known in the art may be used.

Example 3A Mouth spray

45 [0117] Nicotine mouth spray with 14.3 mg nicotine/ml and pH 9.0

Ingredients	mg/ml
Nicotine free base	14.3
50 Ethanol	100.0
Propylene glycol	150.0
Glycerine	25.0
55 L-Arginine	58.3
Sodium Hydrogen Carbonate	14.3
Poloxamer	40.0

(continued)

Ingredients	mg/ml
Levomenthol	10.0
Flavoring agent	4.0
Cooler	3.0
Sweeteners	3.0
Hydrochloric acid	Ad pH 9.0
Purified water	q.s.

Example 3B Mouth spray

Nicotine mouth spray with 14.3 mg nicotine/ml and pH 9

Batch size: 1000 ml

[0118]

Ingredients	mg/ml
Nicotine free base	14.3
Ethanol	100.0
Propylene glycol	150.0
Glycerine	25.0
Glycine comparative or L-Arginine	25.0 or 58.3
Sodium Hydrogen Carbonate	14.3
Poloxamer	40.0
Levomenthol	10.0
Flavouring agent	4.0
Cooler	3.0
Sweeteners	3.0
Hydrochloric acid	Ad pH 9.0
Purified water	q.s.

[0119] In Examples 3A and 3B, and in some of the following Examples, the pH-adjusting capacity of the amino acid buffer is increased by the addition of an adequate amount of pH-adjusting compound.

Manufacturing process:**Mixture I****[0120]**

1. Purified water is charged into a vessel.
 2. Poloxamer is added which shall be solved during mixing before entering next step.
 3. Sweeteners, Glycine (or L-Arginine) and Sodium Hydrogen Carbonate are added.
 4. Continue with the stirring until all components are dissolved.
- Mixture II
5. Ethanol is charged into a vessel.

6. Levomenthol is added and the stirring is ongoing until dissolved.
 7. Propylene glycol, Flavoring agent, Glycerine and Cooler are added. The agitation is continued until the solution is homogeneous.

Final mixing

8. Pour Mixture II into Mixture I and stir until a homogeneous solution is reached.

9. Nicotine is added to the solution while gently stirring.

10. Measure pH of the solution. Adjust pH to 9 by adding Hydrochloric acid.

11. Purified water is added q.s. to batch quantity. The solution is mixed until a clear solution is obtained.

Example 4 Capsules

Nicotine soft capsules 2 mg

[0121]

Ingredients	% (w/w)
<i>Ingredients of Core:</i>	
Nicotine free base	2.2 %
Medium chain triglycerides	86.6%
Flavors and sweeteners	7.8 %
L-Arginine	2.9 %
Colloidal silicon dioxide	0.5 %
<i>Ingredients of Inner Shell:</i>	
Sucrose fatty acid ester	60.0%
Hydrogenated vegetable oil	40.0%
<i>Ingredients of Outer Shell:</i>	
Porcine gelatin	80.0%
Sorbitol	18.0%
Glycerin	2.0%
<i>Weight Ratio:</i>	
Core/Inner shell/Outer shell	64/30/6
Total Capsule weight:	142 mg

Use:

[0122] Seamless soft gel capsules are soft gelatin capsules that are distinguished by their spherical shape and thin, seamless gelatin shell. The thin shell makes the capsules suitable for use in orally dissolving products compared to conventionally produced soft gelatin capsules that are intended to be chewed or swallowed.

Manufacturing process:

[0123] Seamless soft gel capsules are manufactured by formation of droplets consisting of two or more concentric layers. The droplets are formed by feeding different liquids through concentric nozzles. The outermost nozzle feeds a hydrophilic solution consisting of gelatin and additives e.g. plasticizers. The one or more inner nozzles feed a lipophilic liquid (e.g. oils, triglycerides) wherein one or more active substances may be dispersed. The lipophilic centre and hydrophilic perimeter of the formed droplets ensure a good phase separation between shell and core contents. The formed capsules are then subjected to sequential processing steps such as cooling, drying, washing and selection of size and shape.

Example 5A Hard-boiled candies

Nicotine hard-boiled candy with 2 mg nicotine

[0124]

Ingredients	% (w/w)
Purified water	-
Isomalt	78.0
Maltitol 75 % solution	19.5
Nicotine bitartrate dihydrate	0.2
L-Arginine	1.6
Flavor	0.7
Total	100.0

Piece weight 3.5 g

Nicotine /piece 2 mg

Manufacturing process:

[0125]

1. To a stainless steel beaker add purified water, isomalt and maltitol solution. Mix and heat during continuous mixing.
2. Discontinue heating and cool to 135-140 °C. Add nicotine bitartrate dihydrate and mix until fully dispersed. Add L-Arginine and mix at 120 °C until dispersed.
3. Add flavor, mix until uniform.
4. Pour into molds, let cool.

Example 5B Hard-boiled candies

Nicotine hard-boiled candy with 2 mg nicotine

[0126]

Ingredients	% (w/w)
Purified water	
Isomalt	78.0
Maltitol 75 % solution	15.2
Nicotine bitartrate dihydrate	0.6
N-glycylglycine	3.2
Sodium carbonate	1.0
Flavour	2.0
Total	100.0

Piece weight 1.0 g

Nicotine /piece 2 mg

Manufacturing process:**[0127]**

1. To a stainless steel beaker add purified water, isomalt and maltitol solution. Mix and heat during continuous mixing.
2. Discontinue heating and cool to 135-140 °C. Add nicotine bitartrate dihydrate and mix until fully dispersed. Add N-glycylglycine, sodium carbonate and mix at 120 °C until dispersed.
3. Add flavour, mix until uniform.
4. Pour into molds, let cool.

Example 6 Oral films**Nicotine bi-layer film with 2 mg nicotine****[0128]**

Ingredient	mg/film (Active part)	mg/film (Buffer part)
Nicotine free base	2.00	-
Pullulan	30.0	29.9
Xanthan gum	0.04	0.04
Locust bean gum	0.08	0.08
Carrageenan	0.38	0.38
Pectin	0.27	0.27
Polysorbat 80	0.46	0.46
Atmos 300	0.46	0.46
Sucralose	2.10	2.10
Sorbitol	2.90	2.90
Menthol	1.95	1.95
Flavor	12.7	12.7
Colouring agent	0.02	0.02
L-Arginine	-	4.09
Sodium carbonate anhydrous	-	1.23
Tartaric acid	3.7	-
Purified water	About 4.20	About 4.20
Sub-Total	60	60
Total	120	

Manufacturing process (Part 1)**[0129]**

1. Mix together Pullulan, xanthan gum, locust bean gum, carrageenan and pectin.
2. Add heated water to the mixture.
3. Add sucralose and sorbitol, mix to dissolve. Cool to room temperature.
4. Pre-mix Polysorbate 80, Atmos 300, colouring agent, menthol and flavor, and add to the blend.
5. Add tartaric acid and then nicotine free base and mix.
6. Cast Pullulan solution onto substrate of desired thickness and dry with hot air.

Manufacturing process (Part 2):

[0130]

1. Mix together Pullulan, xanthan gum, locust bean gum, carrageenan, pectin, L-Arginine and sodium carbonate.
2. Add heated water to the mixture.
3. Add sucralose and sorbitol, mix to dissolve. Cool to room temperature.
4. Pre-mix Polysorbate 80, Atmos 300, colouring agent, menthol and flavor, and add to the blend
5. Cast Pullulan solution onto substrate of desired thickness and dry with hot air. Manufacturing (Part 3)

1. Cast film (Active) and cast film (Buffer) are laid upon each other and slightly pressed together.

2. Cut into desired size. Size of e.g. 24 mm x 33 mm is appropriate.

[0131] If necessary a barrier layer may be placed between the cast active-containing film and the cast buffer-containing film in order to avoid chemical reactions between these two films.

[0132] Also multi-layer oral films are envisageable.

Example 7 Gummies

Nicotine gummy with 1 mg nicotine

[0133]

Ingredients	g per piece
Isomalt	3.7
Sweetener	1.0
Water	0.1
Pectin	0.1
L-Arginine	0.036
Flavor	0.1
Nicotine bitartrate dihydrate	0.0032
Total	5 g

Manufacturing process:

[0134]

1. Heat the isomalt to melting point and add sweetener and let the mixture cool.
2. To the cooled mixture, add pectin solution, L-Arginine and flavor.
3. Add nicotine bitartrate dihydrate, mix thoroughly.
4. Cast using starch moulds in desired shape and size using methods known in the art.

Example 8 Chewy candies

Nicotine chewy candy with 1 mg nicotine

[0135]

Ingredients	g per piece
Isomalt	3.4
Sweetener	1.0

(continued)

Ingredients	g per piece
Water	0.1
Vegetable oil	0.3
Glycerol monostearate	0.1
L-Arginine	0.036
Flavor	0.1
Nicotine bitartrate dihydrate	0.0032
Total	5 g

Manufacturing process

[0136]

1. Heat the isomalt to melting point and add sweetener and let the mixture cool.
2. To the cooled mixture, add vegetable oil, L-Arginine and flavor. Mix well.
3. Add nicotine bitartrate dihydrate. Mix well. Cast in molds or extrude and cut to desired size using methods known in the art.

Example 9A Compressed chewing gums**Example 9A****Nicotine-containing compressed chewing gum with 2 mg nicotine**

[0137]

Ingredients	Amount in composition (mg)
Nicotine resin complex (NRC) 20%	10
Chewing gum base	556
L-Arginine	36
Sodium carbonate	q. s.
Castor oil	60
Sorbitol	140
Flavoring agents	118
Sweeteners	5
Colloidal silicon dioxide	22.5
Magnesium stearate	20
Talc	22.5
Sodium hydrogen carbonate	q. s.

Manufacturing process:

[0138]

- 1) The nicotine resin complex is blended with the hydrophilic aqueous soluble element, i.e. sorbitol.
- 2) The hydrophobic element, which is practically insoluble in water, i.e. castor oil, is heated to a suitable temperature

until a solution is obtained.

3) The blend obtained in 1) is added to the solution 2) under vigorous stirring.

4) The above blend in 3) is cooled to below room temperature and blended with gum base and other additives.

5) The above blend in 4) is, if necessary, sieved to remove aggregates and compressed into gums by means of direct compression.

Example 9B

Nicotine compressed chewing gum with 2 mg nicotine

[0139]

Ingredients	Amount in composition (mg)
Nicotine resin complex 20%	10
Chewing gum base	300
L-Arginine	36
Sodium carbonate	q.s.
Isomalt	95
Sorbitol	491
Flavouring agents	30
Sweeteners	3
Colloidal silicon dioxide	5
Magnesium stearate	20
Sodium hydrogen carbonate	q.s.

Manufacturing process description:

[0140]

1) Mixing: A gum base powder mixture comprising gum base, sweeteners and glidant is blended with active, flavoring agent, glidant, artificial sweeteners, buffering agents and lubricant.

2) Tableting: The above blend is sieved to remove aggregates if necessary and compressed into gums by means of direct compression.

Example 10 Chewing gums made by mixing, rolling and scoring

[0141]

Ingredients	2 mg Unit formula (mg)	4 mg Unit formula (mg)
Nicotine resin complex 20%	10	20
Chewing gum base	657	650
Xylitol	250	230
L-Arginine	43	65
Flavouring agents	32	22
Levomenthol	2	2
Magnesium oxide	1	1

Manufacturing process:

[0142] Mixing, rolling and scoring is done by a conventional procedure. Double sigma blade mixers are used for mixing

the gum base with the other components of the formulation. The gum base is softened in the mixer. By heat (from the heating jacket) and mixing, the gum base becomes plastic. So, the softened base is mixed with the liquid components and the solid materials as a powder mixture. The warm mass is discharged from the mixer in form of loaves stacked on trays on a truck and stored in a conditioned area until the next step starts. This is to cool the gum.

[0143] After this, the rolling and scoring takes place. The gum is extruded into a thick sheet, which is rolled by multiple sets of calendar rolls to the correct thickness. The scoring rolls, usually two sets, cut the sheet into correctly sized pieces.

[0144] The sheets are then transferred to a conditioned area on trays, where the sheets are cooled to make them brittle enough to be broken. The conditioned gum sheets are then passed through a breaker, which is a rotating drum that parts the sheets into separate pieces of gum along the scores.

[0145] At a sorting stage deformed gums are sorted out. The so accepted gums are further checked by being passed by a metal detector.

Claims

1. A buffered pharmaceutical oral formulation comprising nicotine, **characterized in that** it is buffered with at least one amino acid and/or a salt thereof, and **in that** it comprises a pH-adjusting compound when the pH-adjusting capacity of said at least one amino acid and/or a salt thereof is insufficient; wherein the at least one amino acid and/or a salt thereof comprises an endogenous amino acid which is selected from the group consisting of Arginine, Asparagine, Glutamic acid, Glutamine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Ornithine, Phenylalanine, Serine, Threonine and Valine; and wherein the oral formulation is devoid of tobacco.
2. The oral formulation according to claim 1, **characterized in that** the at least one endogenous amino acid is/are chosen among Asparagine, Glutamic acid, Glutamine, Histidine, Isoleucine, Leucine, Methionine, Phenylalanine, Serine, Threonine and Valine.
3. The oral formulation according to any preceding claim, being buffered in such a way that upon oral administration of the oral formulation to a subject the pH of the saliva of the subject is increased by 0.2 - 4 pH units, or by 0.5 - 2 pH units.
4. The oral formulation according to any preceding claim being buffered with an amino acid together with one or more buffers and/or one or more pH adjusting compounds selected from the group consisting of a carbonate including bicarbonate or sesquicarbonate, glycinate, phosphate, glycerophosphate or citrate of an alkali metal, such as potassium or sodium, or ammonium, including trisodium phosphate, disodium hydrogen phosphate, tripotassium phosphate, dipotassium hydrogen phosphate, and calcium hydroxide, sodium glycinate, trometamol; and mixtures thereof.
5. The oral formulation according to any of claims 1 - 4, wherein the nicotine in any form is selected from the group consisting of a nicotine salt, the free base form of nicotine, a nicotine derivative, such as a nicotine cation exchanger, a nicotine inclusion complex or nicotine in any non-covalent binding; nicotine bound to zeolites; nicotine bound to cellulose or starch micro-spheres; and mixtures thereof.
6. The oral formulation according to claim 5, wherein the nicotine inclusion complex is a cyclodextrin complex, such as β -cyclodextrin.
7. The oral formulation according to claim 5, wherein the nicotine cation exchanger is a polyacrylate cation exchanger.
8. The oral formulation according to claim 5, wherein the nicotine salt is a monotartrate, hydrogen tartrate, citrate, malate and/or hydrochloride salt.
9. The oral formulation according to any of claims 1 - 10, wherein the nicotine in any form is present in an amount of 0.05 - 8 mg or 0.1 - 6 mg or 2 - 5 mg calculated as the free base form of nicotine per unit dose.
10. The oral formulation according to any of claims 1 - 9, wherein optionally at least one or more additive is selected from the group consisting of solvents, co-solvents, stabilisers, preservatives, antioxidants, softeners, thickening agents, binding agents, filling agents, solubilizers, rubbers, lipid barriers, film forming agents, emulsifiers, glidants, lubricants, coating agents, melting vehicles, sweeteners, flavors, aromatics, cooling agents, enhancers, colouring agents, vitamins, minerals, fluorine, breath fresheners, tooth whitening agents and mixtures thereof.

11. The oral formulation according to any of claims 1 - 10 being in the form of a mouth spray, a capsule, a chewing gum, a chewable tablet, a tablet, a melt tablet, a lozenge, a hard boiled candy, a chewy candy, a gummy, or an oral film.
12. The oral formulation according to any of claims 1 - 11 being non-coated.
13. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing tablet comprising nicotine bitartrate dihydrate, an amino acid, mannitol or filling agent, xanthan gum or another binder, croscopovidone or another disintegrant, one or more flavors, and one or more artificial sweeteners.
14. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing melt tablet comprising nicotine bitartrate dihydrate, cocoa powder or another filler/texturizer/taste masker, vegetable oil or another melting vehicle, an amino acid, mannitol or another diluent, soy lecithin or another emulsifier, coloring agent, artificial sweeteners and flavoring agents.
15. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing mouth spray comprising nicotine free base, ethanol or another solvent, an amino acid, poloxamer or another solubilizer, tetracemindinatrium or another stabilizer, and artificial sweeteners.
16. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing soft capsule comprising in the core nicotine free base, medium chain triglycerides or another lipophilic vehicle, flavoring agents, an amino acid, and thickening agent, in the inner shell hydrophilic shell forming materials and in the outer shell forming material and softeners.
17. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing hard boiled candy comprising nicotine bitartrate dihydrate, isomalt, maltitol, an amino acid and flavoring agent.
18. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing oral film comprising nicotine bitartrate dihydrate, xanthan gum, locust bean gum, carrageenan, pectin, pullulan, an amino acid, polysorbate, artificial sweetening agent and flavoring agent.
19. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing gummy comprising nicotine bitartrate dihydrate, isomalt, pectin, an amino acid, artificial sweetening agent and flavoring agent.
20. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing chewy candy comprising nicotine bitartrate dihydrate, isomalt, vegetable oil, an amino acid, sweetening agent and flavoring agent.
21. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing chewing gum being manufactured through direct compressing comprising nicotine resin complex, gum base, an amino acid, and one or more of sweeteners, artificial sweeteners, glidants, flavoring agents and lubricants, and optionally hydrophobic agents.
22. An oral formulation according to any one of claims 1 to 4 wherein the oral formulation is a nicotine-containing chewing gum being manufactured through mixing, rolling and scoring comprising nicotine resin complex, gum base, sweetening agent, flavoring agents and an amino acid.
23. A system for delivering nicotine in any form to a subject, said system comprising an oral formulation according to any of claims 1 - 22 and at least one product comprising nicotine for obtaining reduction of the urge to smoke or use tobacco.
24. The system according to claim 23, wherein the at least one other product is selected from the group consisting of mouth sprays, nasal sprays, transdermal patches, inhaling devices, lozenges, tablets and tobacco.
25. An oral formulation according to claim 1 - 22 for use in obtaining a quick and/or sustained and/or complete reduction of the urge to smoke or use of tobacco and/or for providing a sense of smoking satisfaction without smoking.
26. An oral formulation according to any of claims 1 - 22 for use in delivering nicotine in any form to a subject.

27. A formulation according to any of claims 1 - 22 for use in therapy.
28. A formulation according to claim 27, wherein the therapy is treatment of a disease selected from the group consisting of tobacco or nicotine dependence, Alzheimer's disease, Crohn's disease, Parkinson's disease, Tourette's syndrome, ulcerous colitis and post-smoking-cessation weight control.
29. Use of nicotine for the production of an oral formulation according to any one of claims 1 - 22 for the treatment of a disease selected from the group consisting of tobacco or nicotine dependence, Alzheimer's disease, Crohn's disease, Parkinson's disease, Tourette's syndrome, ulcerous colitis and post-smoking-cessation weight control.

Patentansprüche

1. Gepufferte pharmazeutische orale Formulierung, die Nicotin umfasst, **dadurch gekennzeichnet, dass** sie mit mindestens einer Aminosäure und/oder einem Salz davon gepuffert ist und dass sie eine den pH-Wert einstellende Verbindung umfasst, wenn die pH-Einstellungskapazität der mindestens einen Aminosäure und/oder eines Salzes davon unzureichend ist;
wobei die mindestens eine Aminosäure und/oder ein Salz davon eine endogene Aminosäure aus der Gruppe bestehend aus Arginin, Asparagin, Glutaminsäure, Glutamin, Histidin, Isoleucin, Leucin, Lysin, Methionin, Ornithin, Phenyl-alanin, Serin, Threonin und Valin umfasst und wobei die orale Formulierung tabakfrei ist.
2. Orale Formulierung nach Anspruch 1, **dadurch gekennzeichnet, dass** die mindestens eine endogene Aminosäure aus Asparagin, Glutaminsäure, Glutamin, Histidin, Isoleucin, Leucin, Methionin, Phenyl-alanin, Serin, Threonin und Valin ausgewählt ist.
3. Orale Formulierung nach einem der vorhergehenden Ansprüche, die so gepuffert ist, dass bei oraler Verabreichung der oralen Formulierungen an einen Empfänger der pH-Wert des Speichels des Empfängers um 0,2 - 4 pH-Einheiten oder um 0,5 - 2 pH-Einheiten erhöht wird.
4. Orale Formulierung nach einem der vorhergehenden Ansprüche, die mit einer Aminosäure zusammen mit einem oder mehreren Puffern und/oder einer oder mehreren den pH-Wert einstellenden Verbindungen aus der Gruppe bestehend aus einem Carbonat einschließlich Hydrogencarbonat oder Sesquicarbonat, Glycinat, Phosphat, Glycophosphat oder Citrat von einem Alkalimetall, wie Kalium oder Natrium, oder Ammonium einschließlich Trinatriumphosphat, Dinatriumdihydrogenphosphat, Trikaliumphosphat, Dikaliumdihydrogenphosphat und Calciumhydroxid, Natriumglycinat Trometamol und Mischungen davon gepuffert ist.
5. Orale Formulierung nach einem der Ansprüche 1 - 4, wobei das Nicotin in beliebiger Form aus der Gruppe bestehend aus einem Nicotinsalz, der Form der freien Base von Nicotin, einem Nicotinderivat, wie einem Nicotin-Kationenaustauscher, einem Nicotin-Einschlusskomplex oder Nicotin in einer beliebigen nichtkovalenten Bindung, an Zeolithe gebundenem Nicotin, an Cellulose oder Stärke-Mikrokugeln gebundenem Nicotin und Mischungen davon ausgewählt ist.
6. Orale Formulierung nach Anspruch 5, wobei es sich bei dem Nicotin-Einschlusskomplex um einen Cyclo-dextrin-komplex, wie β -Cyclodextrin, handelt.
7. Orale Formulierung nach Anspruch 5, wobei es sich bei dem Nicotin-Kationenaustauscher um einen Polyacrylat-Kationenaustauscher handelt.
8. Orale Formulierung nach Anspruch 5, wobei es sich bei dem Nicotinsalz um ein Monotartrat-, Hydrogentartrat-, Citrat-, Malat- und/oder Hydrochlorid-Salz handelt.
9. Orale Formulierung nach einem der Ansprüche 1 - 10, wobei das Nicotin in beliebiger Form in einer Menge von 0,05 - 8 mg oder 0,1 - 6 mg oder 2 - 5 mg, berechnet als Form der freien Base von Nicotin, pro Dosis Einheit vorliegt.
10. Orale Formulierung nach einem der Ansprüche 1 - 9, wobei gegebenenfalls mindestens ein oder mehrere Additive aus der Gruppe bestehend aus Lösungsmitteln, Cosolventien, Stabilisatoren, Konservierungsmitteln, Antioxidantien, Weichmachern, Verdickungsmitteln, Bindemitteln, Füllstoffen, Löslichkeitsvermittlern, Kautschuken, Lipidbarrieren, Filmbildnern, Emulgatoren, Gleitmitteln, Schmiermitteln, Beschichtungsmitteln, schmelzenden Vehikeln, Süßungs-

mitteln, Geschmacksstoffen, Aromastoffen, kühlend wirkenden Mitteln, Verstärkern, Farbstoffen, Vitaminen, Mineralien, Fluor, Atemerfrischern, Zahnweißungsmitteln und Mischungen davon ausgewählt werden.

- 5 11. Orale Formulierung nach einem der Ansprüche 1 - 10 in Form eines Mundsprays, einer Kapsel, eines Kaugummis, einer Kautablette, einer Tablette, einer Schmelztablette, einer Lutschtablette, einer Hartkaramelle, einer Weichkaramelle, eines Gummis oder eines oralen Films.
12. Orale Formulierung nach einem der Ansprüche 1 - 11, die unbeschichtet ist.
- 10 13. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um eine Nicotin enthaltende Tablette, die Nicotinbitartratdihydrat, eine Aminosäure, Mannitol oder Füllstoff, Xanthan oder ein anderes Bindemittel, Povidon oder ein anderes Zerfallsmittel, einen oder mehrere Geschmacksstoffe und ein oder mehrere künstliche Süßungsmittel umfasst, handelt.
- 15 14. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um eine Nicotin enthaltende Schmelztablette, die Nicotinbitartratdihydrat, Kakaopulver oder ein/en anderen/s Füllstoff/Texturierungsmittel/Geschmacksmaskierungsmittel, Pflanzenöl oder ein anderes schmelzendes Vehikel, eine Aminosäure, Mannitol oder ein anderes Verdünnungsmittel, Sojalecithin oder einen anderen Emulgator, Farbstoff, künstliche Süßungsmittel und Geschmacksstoffe umfasst, handelt.
- 20 15. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um ein Nicotin enthaltendes Mundspray, das Nicotin in Form der freien Base, Ethanol oder ein anderes Lösungsmittel, eine Aminosäure, Poloxamer oder einen anderen Löslichkeitsvermittler, Tetracemindinatrium oder einen anderen Stabilisator und künstliche Süßungsmittel umfasst, handelt.
- 25 16. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um eine Nicotin enthaltende Weichkapsel, die im Kern Nicotin in der freien Base, mittelkettige Triglyceride oder ein anderes lipophiles Vehikel, Geschmacksstoffe, eine Aminosäure und Verdickungsmittel, in der inneren Hülle hydrophile Schalenbildungsmaterialien und in der äußeren Hülle Außenschalenbildungsmaterial und Weichmacher umfasst, handelt.
- 30 17. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um eine Nicotin enthaltende Hartkaramelle, die Nicotinbitartratdihydrat, Isomalt, Maltitol, eine Aminosäure und Geschmacksstoff umfasst, handelt.
- 35 18. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um einen Nicotin enthaltenden oralen Film, der Nicotinbitartratdihydrat, Xanthan, Johannisbrotkernmehl, Carrageenan, Pektin, Pululan, eine Aminosäure, Polysorbat, künstliches Süßungsmittel und Geschmacksstoff umfasst, handelt.
- 40 19. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um einen Nicotin enthaltenden Gummi, der Nicotinbitartratdihydrat, Isomalt, Pektin, eine Aminosäure, künstliches Süßungsmittel und Geschmacksstoff umfasst, handelt.
- 45 20. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um eine Nicotin enthaltende Weichkaramelle, die Nicotinbitartratdihydrat, Isomalt, Pflanzenöl, eine Aminosäure, Süßungsmittel und Geschmacksstoff umfasst, handelt.
- 50 21. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um einen Nicotin enthaltenden Kaugummi, der durch Direktverpressen hergestellt wird und Nicotin-Harz-Komplex, Kaugummigrundmasse, eine Aminosäure und ein oder mehrere Süßungsmittel, künstliche Süßungsmittel, Gleitmittel, Geschmacksstoffe und Schmiermittel und gegebenenfalls hydrophobe Mittel umfasst, handelt.
- 55 22. Orale Formulierung nach einem der Ansprüche 1 bis 4, wobei es sich bei der oralen Formulierung um einen Nicotin enthaltenden Kaugummi, der durch Mischen, Rollen und Erhitzen hergestellt wird und Nicotin-Harz-Komplex, Kaugummigrundmasse, Süßungsmittel, Geschmacksstoffe und eine Aminosäure umfasst, handelt.
23. System zur Zuführung von Nicotin in beliebiger Form an einen Empfänger, wobei das System eine orale Formulierung nach einem der Ansprüche 1 - 22 und mindestens ein Nicotin umfassendes Produkt umfasst, zur Erzielung einer Verringerung des Drangs zum Rauchen oder zur Verwendung von Tabak.

24. System nach Anspruch 23, wobei das mindestens eine andere Produkt aus der Gruppe bestehend aus Mundsprays, Nasensprays, Transdermalpflastern, Inhalationsvorrichtungen, Lutschtabletten, Tabletten und Tabak ausgewählt ist.
25. Orale Formulierung nach Anspruch 1 - 22 zur Verwendung bei der Erzielung einer schnellen und/oder anhaltenden und/oder vollständigen Verringerung des Drangs zum Rauchen oder zur Verwendung von Tabak und/oder zur Bereitstellung von Rauchbefriedigung ohne Rauchen.
26. Orale Formulierung nach Anspruch 1 - 22 zur Verwendung bei der Zuführung von Nicotin in beliebiger Form an einen Empfänger.
27. Formulierung nach einem der Ansprüche 1 - 22 zur Verwendung bei der Therapie.
28. Formulierung nach Anspruch 27, wobei sich bei der Therapie um die Behandlung einer Erkrankung aus der Gruppe bestehend aus Tabak- oder Nicotinabhängigkeit, Alzheimer-Krankheit, Morbus Crohn, Parkinson-Krankheit, Tourette-Syndrom, Colitis ulcerosa und Gewichtskontrolle nach dem Aufgeben des Rauchens handelt.
29. Verwendung von Nicotin zur Herstellung einer oralen Formulierung nach einem der Ansprüche 1 - 22 zur Behandlung einer Erkrankung aus der Gruppe bestehend aus Tabak- oder Nicotinabhängigkeit, Alzheimer-Krankheit, Morbus Crohn, Parkinson-Krankheit, Tourette-Syndrom, Colitis ulcerosa und Gewichtskontrolle nach dem Aufgeben des Rauchens.

Revendications

1. Formulation orale pharmaceutique tamponnée et comprenant de la nicotine, **caractérisée en ce qu'elle est tamponnée par au moins un acide aminé et/ou un sel de celui-ci, et en ce qu'elle comprend un composé d'ajustement du pH lorsque la capacité d'ajustement du pH dudit au moins un acide aminé et/ou du sel de celui-ci est insuffisante ; caractérisée en ce que le au moins un acide aminé et/ou un sel de celui-ci comprend un acide aminé endogène qui est choisi dans le groupe constitué par l'arginine, l'asparagine, l'acide glutamique, la glutamine, l'histidine, l'isoleucine, la leucine, la lysine, la méthionine, l'ornithine, la phénylalanine, la sérine, la thréonine et la valine ; et caractérisée en ce que la formulation orale est dépourvue de tabac.**
2. Formulation orale selon la revendication 1, **caractérisée en ce que le au moins un acide aminé endogène est choisi parmi l'asparagine, l'acide glutamique, la glutamine, l'histidine, l'isoleucine, la leucine, la méthionine, la phénylalanine, la sérine, la thréonine et la valine.**
3. Formulation orale selon l'une quelconque des revendications précédentes, étant tamponnée de telle façon que, lors de l'administration orale de la formulation orale à un sujet, le pH de la salive du sujet soit augmenté de 0,2-4 unités de pH, ou de 0,5-2 unités de pH.
4. Formulation orale selon l'une quelconque des revendications précédentes, étant tamponnée par un acide aminé conjointement avec un ou plusieurs tampons et/ou un ou plusieurs composés d'ajustement du pH choisis dans le groupe constitué par un carbonate y compris le bicarbonate ou le sesquicarbonate, le glycinate, le phosphate, le glycérophosphate ou le citrate d'un métal alcalin, tel que le potassium ou le sodium, ou l'ammonium, y compris le phosphate insodique, l'hydrogénophosphate disodique, le phosphate tripotassique, l'hydrogénophosphate dipotassique, et l'hydroxyde de calcium, le glycinate de sodium, le trométamol ; et des mélanges de ceux-ci.
5. Formulation orale selon l'une quelconque des revendications 1-4, **caractérisée en ce que la nicotine sous une forme quelconque est choisie dans le groupe constitué par un sel de nicotine, la forme de base libre de nicotine, un dérivé de nicotine, tel qu'un échangeur de cation de nicotine, un complexe d'inclusion de nicotine ou de la nicotine selon une fixation non covalente quelconque ; la nicotine fixée à des zéolithes ; la nicotine fixée à de la cellulose ou des microsphères d'amidon ; et des mélanges de ceux-ci.**
6. Formulation orale selon la revendication 5, **caractérisée en ce que le complexe d'inclusion de nicotine est un complexe de cyclodextrine, telle que la β -cyclodextrine.**
7. Formulation orale selon la revendication 5, **caractérisée en ce que l'échangeur de cations de nicotine est un échangeur de cations à base de polyacrylate.**

8. Formulation orale selon la revendication 5, **caractérisée en ce que** le sel de nicotine est un sel de monotartrate, hydrogéntartrate, citrate, malate et/ou chlorhydrate.
- 5 9. Formulation orale selon l'une quelconque des revendications 1-10, **caractérisée en ce que** la nicotine sous une forme quelconque est présente selon une quantité de 0,05-8 mg ou 0,1-6 mg ou 2-5 mg, calculée comme forme de base libre de nicotine par dose unitaire.
- 10 10. Formulation orale selon l'une quelconque des revendications 1-9, **caractérisée en ce qu'éventuellement** au moins un ou plusieurs additifs sont choisis dans le groupe constitué par les solvants, les co-solvants, les stabilisants, les conservateurs, les antioxydants, les adoucissants, les épaississants, les liants, les charges, les agents solubilisants, les caoutchoucs, les barrières lipidiques, les agents filmogènes, les émulsifiants, les agents glissants, les lubrifiants, les agents d'enrobage, les véhicules fondants, les édulcorants, les arômes, les substances aromatiques, les agents rafraîchissants, les exhausteurs, les agents colorants, les vitamines, les minéraux, le fluor, les rafraîchisseurs d'haleine, les agents de blanchiment des dents, et des mélanges de ceux-ci.
- 15 11. Formulation orale selon l'une quelconque des revendications 1-10, se trouvant sous la forme d'un spray oral, d'une capsule, d'un chewing-gum, d'un comprimé croquable, d'un comprimé, d'un comprimé fondant, d'une tablette, d'un bonbon croquant, d'un bonbon mou, d'un bonbon gélifié, ou d'un film oral.
- 20 12. Formulation orale selon l'une quelconque des revendications 1-11, qui est non enrobée.
13. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un comprimé contenant de la nicotine comprenant du bitartrate de nicotine dihydraté, un acide aminé, du mannitol ou une charge, de la gomme xanthane ou un autre liant, de la crospovidone ou un autre agent déliant, un ou
- 25 plusieurs arômes, et un ou plusieurs édulcorants artificiels.
14. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un comprimé prodispersible contenant de la nicotine, comprenant du bitartrate de nicotine dihydraté, de la poudre de cacao ou un(e) autre charge/agent texturant/masqueur de goût, une huile végétale ou un autre véhicule fondant,
- 30 un acide aminé, du mannitol ou un autre diluant, de la lécithine de soja ou un autre émulsifiant, un agent colorant, des édulcorants artificiels et des agents aromatisants.
15. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un spray oral contenant de la nicotine, comprenant une base libre de nicotine, de l'éthanol ou un autre solvant,
- 35 un acide aminé, un poloxamère ou un autre stabilisant, tetracemindinium ou un autre stabilisant, et des édulcorants artificiels.
16. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est une capsule molle contenant de la nicotine, comprenant dans le cœur une base libre de nicotine, des triglycérides à chaîne moyenne ou un autre véhicule lipophile, des agents aromatisants, un acide aminé, et un épaississant,
- 40 dans l'enveloppe interne des matériaux de formation d'une enveloppe hydrophile et dans l'enveloppe externe un matériau de formation et des adoucissants.
17. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un bonbon dur contenant de la nicotine, comprenant du bitartrate de nicotine dihydraté, de l'isomalt, du mannitol,
- 45 un acide aminé et un agent aromatisant.
18. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un film oral contenant de la nicotine, comprenant du bitartrate de nicotine dihydraté, de la gomme xanthane, de la gomme de caroube, un carraghénane, une pectine, un pullulane, un acide aminé, du polysorbate, un agent
- 50 édulcorant artificiel et un agent aromatisant.
19. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un bonbon gélifié contenant de la nicotine, comprenant du bitartrate de nicotine dihydraté, de l'isomalt, une
- 55 pectine, un acide aminé, un agent édulcorant artificiel et un agent aromatisant.
20. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un bonbon mou contenant de la nicotine, comprenant du bitartrate de nicotine dihydraté, de l'isomalt, de l'huile

végétale, un acide aminé, un agent édulcorant et un agent aromatisant.

21. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un chewing-gum contenant de la nicotine fabriqué par compression directe, comprenant un complexe de résine de nicotine, une base de gomme, un acide aminé, et un ou plusieurs parmi des agents édulcorants, des agents édulcorants artificiels, des agents glissants, des agents aromatisants et des lubrifiants, et éventuellement des agents hydrophobes.
22. Formulation orale selon l'une quelconque des revendications 1 à 4, **caractérisée en ce que** la formulation orale est un chewing-gum contenant de la nicotine fabriqué par malaxage, laminage et découpage, comprenant un complexe de résine de nicotine, une base de gomme, un agent édulcorant, des agents aromatisants et un acide aminé.
23. Système d'administration de nicotine sous une forme quelconque à un sujet, ledit système comprenant une formulation orale selon l'une quelconque des revendications 1-22 et au moins un produit comprenant de la nicotine pour l'obtention d'une réduction de l'envie de fumer ou d'utiliser du tabac.
24. Système selon la revendication 23, **caractérisé en ce que** le au moins un autre produit est choisi dans le groupe constitué par un spray oral, un spray nasal, un patch transdermique, un dispositif d'inhalation, une tablette, un comprimé et du tabac.
25. Formulation orale selon les revendications 1-22, pour une utilisation dans l'obtention d'une réduction rapide et/ou prolongée et/ou complète de l'envie de fumer ou d'utiliser du tabac et/ou pour la fourniture d'une sensation de satisfaction de fumer, sans fumer.
26. Formulation orale selon l'une quelconque des revendications 1-22, pour une utilisation dans l'administration de nicotine sous une forme quelconque à un sujet.
27. Formulation selon l'une quelconque des revendications 1-22, pour une utilisation en thérapie.
28. Formulation selon la revendication 27, **caractérisée en ce que** la thérapie est le traitement d'une maladie choisie dans le groupe constitué par la dépendance au tabac ou à la nicotine, la maladie d'Alzheimer, la maladie de Crohn, la maladie de Parkinson, le syndrome de Tourette, la rectocolite hémorragique, et le contrôle pondéral après l'arrêt du tabac.
29. Utilisation de nicotine pour la production d'une formulation orale selon l'une quelconque des revendications 1-22, pour le traitement d'une maladie choisie dans le groupe constitué par la dépendance au tabac ou à la nicotine, la maladie d'Alzheimer, la maladie de Crohn, la maladie de Parkinson, le syndrome de Tourette, la rectocolite hémorragique, et le contrôle pondéral après l'arrêt du tabac.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 5810018 A [0011]
- US 5939100 A [0011]
- US 4967773 A [0011]
- US 4579858 A [0012]
- DE 3241437 [0012]
- WO 9312764 A [0012]
- US 5167242 A [0014]
- US 3877468 A [0015]
- US 3901248 A [0015]
- US 3845217 A [0016] [0070]
- WO 02102357 A [0016] [0017]
- WO 2005023227 A [0017]
- WO 03055486 A [0019]
- US 5733572 A [0022]

Non-patent literature cited in the description

- *MMWR*, 1997, vol. 46, 1217-1220 [0004]
- RUSSELL et al. *British Medical Journal*, 1983, vol. 286, 683 [0012]
- JARVIS et al. *Brit. J. of Addiction*, 1987, vol. 82, 983 [0012]
- ROSE. *Pharmacologic Treatment of Tobacco Dependence*. Harvard Univ. Press, 1986, 158-166 [0013]
- OQAWA TAZUKO et al. Screening of bitterness-suppressing agents for quinine: The use of molecularly imprinted polymers. *Journal of Pharmaceutical Sciences*, February 2005, vol. 94 (2), 353-362 [0018]

Electronic Acknowledgement Receipt

EFS ID:	26696046
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	19-AUG-2016
Filing Date:	28-OCT-2015
Time Stamp:	15:50:09
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment		no			
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		13211-713-303_IDS_Filing_8-19-2016.pdf	345145	yes	5
			109e549322c0c28093e728b7d6b9346eec7994d6		

	Multipart Description/PDF files in .zip description								
	Document Description		Start	End					
	Transmittal Letter		1	3					
	Information Disclosure Statement (IDS) Form (SB08)		4	5					
Warnings:									
Information:									
2	Foreign Reference	EP2152313B.pdf	8630620	no	28				
			b964bc79855e9ccb2a5804467fe593d8436850d8						
Warnings:									
Information:									
Total Files Size (in bytes):			8975765						
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>									

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8

I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on August 19, 2016.

/Brian Flick/

Name

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 14/925,968 Confirmation No.: 2707
 First Named Inventor : Adam Bowen
 Filed : October 28, 2015
 Art Unit : 1747
 Examiner : Mayes, Dionne Walls
 Title : NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES
 AND METHODS THEREOF
 Customer No. : 66854

INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.97 & § 1.98

Sir:

In accordance with 37 CFR § 1.97-1.98, applicants hereby submit an Information Disclosure Statement, including attached forms(s) PTO/SB/08. A copy of each reference is being submitted herewith, along with a concise explanation in English for those publications in a foreign language.

Applicants respectfully request that the listed information be considered by the Examiner and be made of record in the above-identified application. Applicants further request that the Examiner initial and return a copy of the attached form(s) PTO/SB/08 in accordance with MPEP §609.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and /or to prove that this information may not be enabling for the teachings purportedly offered.

This statement is not intended to represent that a search has been made or that the information cited in the statement is, or is considered to be, prior art or material to patentability as defined in 37 CFR §1.56.

FILING OF INFORMATION DISCLOSURE STATEMENT



37 CFR §1.97(b)

This statement is being submitted under 37 CFR §1.97(b) because the IDS is being filed:

- ☐ 1). Within 3 months of the application filing date, or
- ☐ 2). Within 3 months of entry of a national stage as set forth in § 1.491, or
- ☐ 3). Before the mail date of a first Office Action on the merits, or
 - ☐ 3a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below
- ☒ 4). Before the mailing of a first Office Action after filing a request for continued examination under § 1.114.
 - ☐ 4a). Certifications as specified in § 1.97(e) and § 1.704(d) are provided below

☐ **37 CFR § 1.97(c)**

This statement is being filed after the latest of:

- ☐ 1). Three months beyond the filing date of a national application, or
- ☐ 2). Three months beyond the date of entry of the national stage as set forth in § 1.491 in an international application, or
- ☐ 3). The mailing date of a first Office Action on the merits, but before the mailing date of the earlier of a final Office Action under § 1.113 or a Notice of Allowance under § 1.311, and then either:
 - ☐ A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or included with the payment of other papers filed together with this statement.
 - or
 - ☐ B). A certification as specified in § 1.97(e) is provided below; thus no fee is required.

☐ **37 CFR § 1.97(d)**

This statement is being filed after the mailing date of a Final Office action, a Notice of Allowance under § 1.311, or an action that otherwise closes prosecution, but on or before payment of the issue fee, and then:

A). A fee of \$180 (\$90 for small entity) as set forth in § 1.17(p) is authorized below, enclosed, or payment is included with other papers filed together with this statement

--AND--

B). A certification as specified in § 1.97(e) is included below.

CONTENT OF INFORMATION DISCLOSURE STATEMENT UNDER
37 CFR § 1.98

☒ **37 CFR §1.98 (a)(2)(ii), U.S. patents or patent application publication(s) cited**

- ☒ 1). Since not requested by the Office, U.S. patents and U.S. patent application publications are not included.
- ☐ 2). At the request of the Office, a copy of the following U.S. patent or patent application publication is attached:
- ☒ 3). Items identified by a double asterisk (**) on the SB08A are *commonly-owned U.S. patents and U.S. patent application publications.

☒ **37 CFR §1.98 (a)(2)(iii) and (d), *Commonly-owned, unpublished U.S. applications cited**

- ☐ 1). A copy of each application specification including the claim(s), and any drawing, or that portion of the application that caused it to be listed, is attached.
- ☐ 2). A copy of each application specification is not submitted because the specification was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:
- ☒ 3). A copy of each application specification is not submitted because the application is stored in the IFW.

**Applicant(s) assume the Examiner has access to the file histories of these items. However, if the Examiner would like to receive copies of Office Actions in any of the commonly-owned applications, publications and/or patents identified on the attached SB08, please inform the undersigned and copies will be provided.*

☐ **37 CFR §1.98 (a)(2)(iii) and (d), English language publication (other than U.S. patents, patent applications, or pending unpublished applications) cited**

- ☐ 1). A legible copy of each publication or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each publication or that portion which caused it to be listed is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

☒ **37 CFR §1.98 (a)(2)(i) and (d), Foreign patent(s) in English cited**

- ☒ 1). A legible copy of each foreign patent or that portion which caused it to be listed is attached.
- ☐ 2). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

☐ **37 CFR §1.98 (a)(2)(i), (a)(3)(i-ii) and 609.04(a)III, Foreign patent(s) or other foreign documents not in English cited. Either:**

- ☐ 1). A legible copy of each foreign patent, each publication or that portion which caused it to be listed, is attached **--AND--**
- ☐ 2a). An English language abstract or an English language copy of a foreign search report or other action by a foreign patent office is provided herewith to fulfill the requirement for a concise explanation of the relevance, as it is presently understood by the individual designated in § 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language: Cite no(s): **--AND/OR--**
- ☐ 2b). A copy of a written, English-language translation or portion thereof is readily available and attached: Cite no(s): **--OR--**
- ☐ 3). A copy of each foreign patent is not submitted because the publication was previously submitted in the IDS of the following, earlier filed application relied on for an earlier effective filing date:

STATEMENT UNDER 37 CFR § 1.97(e)

☐ Each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. Cite no(s):

☐ No item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement. Cite no(s):

STATEMENT UNDER 37 CFR § 1.704(d)

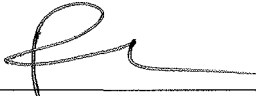
☐ Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

FEE AUTHORIZATION

☒ The Commissioner is hereby authorized to charge the above-referenced fees of \$0.00 and charge any additional fees or credit any overpayment associated with this communication to Deposit Account No. 50-4050.

Respectfully Submitted,

Dated: August 19, 2016

By: 
Richard D. Shoop, Reg. No. 45,763

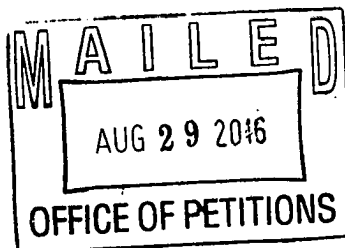
Shay Glenn LLP
2755 Campus Drive, Suite 210
San Mateo, CA 94403
(650) 212-1700
Customer No. 66854



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

SHAY GLENN LLP
2755 CAMPUS DRIVE
SUITE 210
SAN MATEO CA 94403



Doc Code: TRACK1.GRANT

Decision Granting Request for Prioritized Examination (Track I or After RCE)	Application No.: 14/925,968
<p>1. THE REQUEST FILED <u>August 19, 2016</u> IS GRANTED.</p> <p>The above-identified application has met the requirements for prioritized examination</p> <p>A. ☐ for an original nonprovisional application (Track I).</p> <p>B. ☒ for an application undergoing continued examination (RCE).</p> <p>2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:</p> <p>A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply;</p> <p>B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim;</p> <p>C. filing a <u>request for continued examination</u>;</p> <p>D. filing a notice of appeal;</p> <p>E. filing a request for suspension of action;</p> <p>F. mailing of a notice of allowance;</p> <p>G. mailing of a final Office action;</p> <p>H. completion of examination as defined in 37 CFR 41.102; or</p> <p>I. abandonment of the application.</p> <p>Telephone inquiries with regard to this decision should be directed to Brian W. Brown at 571-272-5338.</p> <p>/Brian W. Brown/ [Signature]</p> <p>Petitions Examiner, Office of Petitions (Title)</p>	

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8	
I hereby certify that this correspondence is being transmitted to the USPTO via EFS-Web on September 12, 2016.	
/Mary Buggie/	9/12/2016
Mary Buggie	Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707

First Named Inventor : Adam BOWEN

Filing Date : October 28, 2015

Art Unit : 1747

Examiner : Mayes, Dionne Walls

Title : NICOTINE SALT FORMULATIONS FOR AEROSOL
DEVICES AND METHODS THEREOF

Customer No. : 66854

Mail Stop 16
 Director of the United States Patent and Trademark Office
 P.O. Box 1450
 Alexandria, VA 22313-1450

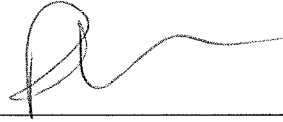
REQUEST FOR REFUND UNDER 37 C.F.R. § 1.28

On June 15, 2016 and July 12, 2016, Applicants electronically filed Information Disclosure Statements via the Electronic Filing System (EFS). The undiscounted fees of \$180 were paid via Deposit Account No. 50-4050. **Applicants hereby assert small entity status**, as shown in the copy of the Change Entity Status electronically submitted on August 17, 2016. Therefore, Applicants request a refund of \$180 to Deposit Account No. 50-4050.

ITEMIZATION			
Fee Description	Undiscounted Entity Amount Previously Paid	Current Small Entity Fees	Refund Requested
Information Disclosure Statement	\$180 on June 22, 2016	\$90	\$90
Information Disclosure Statement	\$180 on July 12, 2016	\$90	\$90
Total Refund Requested to Deposit Account No. 50-4050:			\$180

If it is determined that a telephone conference would expedite the processing of this Request, please contact the undersigned at the number given below.

Respectfully submitted,



Date: September 12, 2016

Richard D. Shoop
Reg. No. 45,763

SHAY GLENN LLP
2755 CAMPUS DRIVE, SUITE 210
SAN MATEO, CA 94403
TELEPHONE: 650.212.1700
FACSIMILE: 650.212.7562

Change Entity Status - Confirmation

Request ID 23382
Timestamp Aug 17, 2016 9:03:31 PM EST
Status Submitted

The Entity Status of the application has been successfully changed

Application Number 14/925,968
Attorney Docket Number 13211-713.303
Title NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
Updated Entity Status Small
Micro certification statement N/A

I certify, in accordance with 37 CFR 1.4(d)(4):

 I am an attorney or agent registered to practice before the Patent and Trademark Office who has been given power of attorney in this application

Filed By Richard D. Shoop
Registration Number 45763

Signatures	Signature	Name
	/Richard D. Shoop/	Richard D. Shoop

Point of Contact Info

Name Richard D. Shoop
Telephone (650) 212-1700
Email rick@shayglenn.com

Electronic Acknowledgement Receipt

EFS ID:	26900696
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Mary Buggie
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	12-SEP-2016
Filing Date:	28-OCT-2015
Time Stamp:	17:47:23
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
------------------------	----

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Refund Request	13211-713-303_RequestRefund.pdf	84268 99596b2c375e9deb6c2bd1d6da8800817b0149ff	no	3

Warnings:

Information:	
Total Files Size (in bytes):	84268
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>	

USPTO
RECEIPTS ACCOUNTING
DIVISION

CERTIFICATE OF TRANSMISSION UNDER 37 CFR 1.8
I hereby certify that this correspondence is being transmitted to
the USPTO via EFS-Web on September 12, 2016.

/Mary Buggie/ 9/12/2016
Mary Buggie Date

2016 SEP 12 AM 9:14

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 14/925,968 Confirmation No. : 2707
First Named Inventor : Adam BOWEN
Filing Date : October 28, 2015
Art Unit : 1747
Examiner : Mayes, Dionne Walls
Title : NICOTINE SALT FORMULATIONS FOR AEROSOL
DEVICES AND METHODS THEREOF
Customer No. : 66854

Mail Stop 16
Director of the United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR REFUND UNDER 37 C.F.R. § 1.28

On June 15, 2016 and July 12, 2016, Applicants electronically filed Information Disclosure Statements via the Electronic Filing System (EFS). The undiscounted fees of \$180 were paid via Deposit Account No. 50-4050. Applicants hereby assert small entity status, as shown in the copy of the Change Entity Status electronically submitted on August 17, 2016. Therefore, Applicants request a refund of \$180 to Deposit Account No. 50-4050.

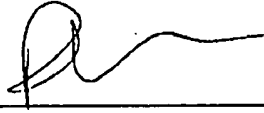
ITEMIZATION			
Fee Description	Undiscounted Entity Amount Previously Paid	Current Small Entity Fees	Refund Requested
Information Disclosure Statement	\$180 on June 22, 2016	\$90	\$90
Information Disclosure Statement	\$180 on July 12, 2016	\$90	\$90
Total Refund Requested to Deposit Account No. 50-4050:			\$180

- 1 of 2 -

SG Docket No.: 13211-713.303

If it is determined that a telephone conference would expedite the processing of this Request, please contact the undersigned at the number given below.

Respectfully submitted,



Date: September 12, 2016

Richard D. Shoop
Reg. No. 45,763

SHAY GLENN LLP
2755 CAMPUS DRIVE, SUITE 210
SAN MATEO, CA 94403
TELEPHONE: 650.212.1700
FACSIMILE: 650.212.7562

Electronic Acknowledgement Receipt

EFS ID:	26322723
Application Number:	14925968
International Application Number:	
Confirmation Number:	2707
Title of Invention:	<p>NICOTINE SALT FORMULATIONS FOR AEROSOL DEVICES AND METHODS THEREOF</p> <p>09/20/2016 SSANDARA 00000004 504050 14925968 01 FC:2806 90.00 DA</p> <p>09/20/2016 SSANDARA 00000005 504050 14925968 01 FC:2806 90.00 DA</p>
First Named Inventor/Applicant Name:	Adam BOWEN
Customer Number:	66854
Filer:	Richard Douglas Shoop/Brian Flick
Filer Authorized By:	Richard Douglas Shoop
Attorney Docket Number:	13211-713.303
Receipt Date:	12-JUL-2016
Filing Date:	28-OCT-2015
Time Stamp:	12:51:13
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$180
RAM confirmation Number	071216INTEFSW00011347504050
Deposit Account	504050
Authorized User	Richard Shoop
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <div style="display: flex; justify-content: space-between;"> <div> <p>Adjustment date: 09/20/2016 SSANDARA</p> <p>06/16/2016 INTEFSW 00002820 504050 14925968</p> <p>01 FC:1806 180.00 CR</p> </div> <div> <p>Adjustment date: 09/20/2016 SSANDARA</p> <p>07/12/2016 INTEFSW 00011347 504050 14925968</p> <p>01 FC:1806 180.00 CR</p> </div> </div>	

Substitute for form 1449/PTO

(Use as many sheets as necessary)

Sheet	1	of	2
-------	---	----	---

Application Number	14/925,968
Filing Date	October 28, 2015
First Named Inventor	Adam Bowen
Art Unit	1747
Examiner Name	Mayes, Dionne Walls
Attorney Docket Number	13211-713.303

[illegible]

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ ~Number ⁴ ~Kind Code ⁵ (if known)				
	687	EP0283672B1	9/22/1993	R J Reynolds Tobacco		
	688	EP2319934B1	9/2/2015	Stichting Dienst		
	689	WO2007/078273A1	7/12/2007	Augite Inc.		
	690	WO2015/009862A2	1/22/2015	Altria Client Services		

Examiner
Signature

Date	
Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Complete if Known			
		Application Number	14/925,968		
		Filing Date	October 28, 2015		
		First Named Inventor	Adam Bowen		
		Art Unit	1747		
		Examiner Name	Mayes, Dionne Walls		
Sheet	2	of	2	Attorney Docket Number	13211-713.303

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	683	BURCH et al.; Effect of pH on nicotine absorption and side effects produced by aerosolized nicotine; Journal of Aerosol Medicine: Deposition, Clearance, and Effects in the Lung; 6(1); pp. 45-52; 1993	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

(19)



Europäisches Patentamt
European Patent Office
Office européen des brevets



(11)

Publication number:

0 283 672 B1

(12)

EUROPEAN PATENT SPECIFICATION

(45)

Date of publication of patent specification: **22.09.93**

(51)

Int. Cl.⁵: **A24B 15/30**

(21)

Application number: **88101280.1**

(22)

Date of filing: **29.01.88**

(54)

Cigarette.

(30)

Priority: **10.02.87 US 12922**
24.12.87 US 137987

(43)

Date of publication of application:
28.09.88 Bulletin 88/39

(45)

Publication of the grant of the patent:
22.09.93 Bulletin 93/38

(84)

Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

(56)

References cited:
EP-A- 0 103 970
DE-A- 1 517 331
FR-A- 2 182 367
FR-A- 2 403 035
FR-A- 2 527 055

**J.C. LEFFINGWELL et al.: "Tobacco Flavoring
for Smoking Products", 1972, pages 10,13,
R.J. REYNOLDS TOBACCO CO., Winston-
Salem, N.C., US**

(73)

Proprietor: **R.J. REYNOLDS TOBACCO COM-
PANY**
401 North Main Street
Winston-Salem North Carolina 27102(US)

(72)

Inventor: **Lawson, Jerry Wayne**
112 Spillsbury Court
Clemmons, N.C. 27012(US)
Inventor: **Bullings, Bruce Randall**
1423 Butler Street
Winston-Salem, N.C. 27102(US)
Inventor: **Perfetti, Thomas Albert**
2116 Newcastle Drive
Winston-Salem, N.C. 27103(US)

(74)

Representative: **Hoeger, Stellrecht & Partner**
Uhlandstrasse 14 c
D-70182 Stuttgart (DE)

EP 0 283 672 B1

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid (Art. 99(1) European patent convention).

Description

The present invention relates to cigarettes and other such types of smoking articles.

Cigarettes are popular smoking articles which have a substantially cylindrical rod shaped structure and include a charge of tobacco (i.e., in cut filler form) surrounded by a wrapper such as paper thereby forming a tobacco rod. Currently, popular cigarettes include blends of tobacco materials, the majority of the blends having nicotine contents in the range from about 1.2 percent to about 2.25 percent, more frequently from about 1.4 percent to about 2 percent, and most frequently from about 1.6 percent to about 1.8 percent, based on the dry weight of the tobacco materials. It has become desirable to manufacture cigarettes having cylindrical filters aligned in an end-to-end relationship with the tobacco rod. Typically, filters are manufactured from fibrous materials such as cellulose acetate and are attached to the tobacco rod using a circumscribing tipping material.

Popular cigarettes classified as "full flavor" cigarettes deliver a desirable tobacco taste, flavor and satisfaction to the smoker. Typically, the "full flavor" cigarettes deliver about 14 mg or more of FTC "tar" per cigarette. A second classification of popular cigarettes is the "full flavor low tar" classification. Typically, the "full flavor low tar" cigarettes deliver from about 8 to about 14 mg of FTC "tar" per cigarette, as well as lower levels of FTC nicotine as compared to "full flavor" cigarettes. A third classification of popular cigarettes is the "ultra low tar" classification. Such "ultra low tar" cigarettes deliver still lower levels of FTC "tar" and nicotine. Typically, the "ultra low tar" cigarettes deliver less than about 7 mg of FTC "tar" per cigarette. The "full flavor low tar" and "ultra low tar" cigarettes conventionally have air dilution means such as laser perforations provided in the periphery of the mouthend region thereof, or have filter elements highly efficient for the removal of "tar" and nicotine from the mainstream aerosol.

In general, the perceived taste or strength of the cigarettes classified as having lower levels of "tar" and nicotine are progressively less than that of the cigarettes which are classified as approaching the characteristics of the "full flavor" cigarettes. It has been proposed to add numerous flavorants to the cut filler of lower "tar" cigarettes to enhance the taste, strength and satisfaction of such cigarettes. However, such addition generally yields mainstream smoke which may be perceived as harsh or irritating to the mouth, nose and throat of the user. By the publication "Tobacco Flavoring for Smoking Products" published in 1972 by R. J. Reynolds Tobacco Company, pages 10 and 13 it had been proposed to apply a flavorant in the form of Levulinic acid to tobacco, tobacco substitutes, filters and the like of a smoking product in order to add body to the smoke and to create a sweet, caramel smoke taste.

Additionally, it is possible to employ tobaccos having a naturally high nicotine content as cut filler to enhance the tobacco taste, strength and satisfaction of such cigarettes. However, cigarettes having high nicotine contents (eg., which include tobacco blends having natural nicotine contents above about 2.25 weight percent) generally have the propensity to yield unpalatable mainstream smoke which may be perceived as harsh or irritating to the mouth, nose and throat of the user.

It is therefore an object of this invention to improve the smoking character of such cigarettes so that their smoke is perceived as not being overly harsh or irritating. In particular it would be desirable to provide a cigarette such as an "ultra low tar" cigarette which is capable of delivering a good tobacco taste, strength and smoking satisfaction characteristic of a "full flavor low tar" cigarette while being perceived as palatable but not as overly harsh or irritating. In addition, it would be desirable to provide a cigarette such as a "full flavor low tar" cigarette which is capable of delivering a good tobacco taste, strength and smoking satisfaction characteristic of a "full flavor" cigarette while being perceived as palatable but not as overly harsh or irritating. Furthermore, it would be desirable to improve the smoking character of cigarettes which employ tobaccos or other tobacco materials having a wide range of nicotine contents.

This object is achieved by a cigarette as defined in claim 1.

The present invention relates to a smoking article which delivers good tobacco taste while being capable of delivering relatively low amounts of FTC "tar." Preferred articles of this invention are cigarettes which deliver taste, strength and smoking satisfaction characteristic of "full flavor" cigarettes, and relatively low levels of FTC "tar" characteristic of "full flavor low tar" cigarettes. Also preferred are cigarettes which deliver taste, strength and smoking satisfaction characteristic of "full flavor low tar" cigarettes, and relatively low levels of FTC "tar" characteristic of "ultra low tar" cigarettes. In addition, the preferred cigarettes are extremely palatable and provide the perception of having a smooth smoking character (i.e., not providing a perceived harsh or irritating character) relative to a comparable cigarette delivering similar levels of FTC "tar." Of particular interest are cigarettes having (i) relatively low FTC "tar" to FTC nicotine ratios, (ii) relatively low FTC carbon monoxide to FTC nicotine ratios, (iii) good tobacco flavor, strength and satisfaction, and (iv) a smooth, palatable smoking character without being overly mild tasting.

Generally, the levulinic acid is an additive to at least a portion of the smokable material. The acid can be present within the cigarette in a dissociated and/or nondissociated form. The levulinic acid can be present within the cigarette as levulinic acid and/or levulinate ion.

As used herein, the term "dry weight" in referring to the smokable material of the smoking article is meant the mass of the smokable material after being dried to constant weight at 214 °F (101 °C) for 3 hours in a force-draft oven. See, Moseley et al, Ind. Eng. Chem., Vol. 43, p. 2342 (1951).

As used herein, the term "nicotine content" in referring to the smokable material is meant the mass alkaloid nicotine as analyzed and quantitated by spectroscopic techniques divided by the dry weight of the smokable material analyzed. See, Harvey et al, Tob. Sci., Vol. 25, p. 131 (1981).

The smokable material from which cigarettes of this invention are manufactured conveniently can be a cut filler material composed of one or more tobacco materials having a naturally high nicotine content. The naturally high nicotine content tobacco material(s) can be employed alone or as blends with (i) one or more tobacco materials having low nicotine contents, and/or (ii) one or more tobacco substitutes. As such, cigarettes of this invention include those cigarettes wherein the smokable material thereof exhibits a total nicotine content or blend nicotine content above about 2.25 percent.

A cigarette in accord with this invention conveniently can have incorporated therein at least one salt provided from nicotine and an organic acid. The salt is incorporated within the cigarette as an additive. Preferably, the salt is such that the molar ratio of nicotine to organic acid therein is 1:3. Most preferably, the salt additive includes nicotine levulinate. The particular salt is incorporated into the cigarette in such a manner that during use of the cigarette, the salt is subjected to decomposition conditions. For example, a cigarette of this invention can include a smokable material as well as at least one salt of nicotine and an organic acid as an additive, wherein (i) the nicotine content of the cigarette is above about 2.25 percent, based on the dry weight of the smokable material, and (ii) one of the aforementioned salts is nicotine levulinate.

The presence of the nicotine/levulinic acid salt within the cigarette provides improved tobacco taste, strength and smoking satisfaction as well as improved or maintained flavor characteristics to the aerosol during use of the article while avoiding undesirable off-tastes during use.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 is a longitudinal sectional view of a cigarette of this invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

One embodiment of this invention is shown in Figure 1 and has the form of a cigarette 10. The cigarette includes a generally cylindrical rod 15 of smokable material 20, such as tobacco cut filler, contained in circumscribing outer wrapping material 25. The rod 15 is hereinafter referred to as a "tobacco rod." The ends of the tobacco rod are open to expose the smokable material. The cigarette 10 also includes a filter element 30 positioned adjacent one end of the tobacco rod 15 such that the filter element and tobacco rod are axially aligned in an end-to-end relationship, preferably abutting one another. Filter element 30 has a generally cylindrical shape, and the diameter thereof is essentially equal to the diameter of the tobacco rod. The ends of the filter element are open to permit the passage of air and smoke therethrough. The filter element 30 includes filter material 35 which is overwrapped along the longitudinally extending surface thereof with circumscribing plug wrap material 40.

The filter element 30 is attached to the tobacco rod 15 by tipping material 45 which circumscribes both the entire length of the filter element and an adjacent region of the tobacco rod. The inner surface of the tipping material 45 is fixedly secured to the outer surface of the plug wrap 40 and the outer surface of the wrapping material 25 of the tobacco rod, using a suitable adhesive. If desired, a ventilated or air diluted cigarette is provided with an air dilution means such as a series of perforations 50 each of which extend through the tipping material and plug wrap.

Typically, the tobacco rod has a length which ranges from about 50 mm to about 85 mm, a circumference of about 17 mm to about 27 mm; and the wrapping material thereof is a conventional cigarette wrapping paper. Suitable cigarette wrapping papers are commercially available as Reference Nos. 719 and 856 from Kimberly-Clark Corp. or as Ecusta Experimental Nos. TOD 01788 and TOD 03363 from Ecusta Corp. If desired a dual wrapper system can be employed. The tobacco rods and the resulting cigarettes can be manufactured in any known configuration using known cigarette making techniques and equipment.

Typically, the filter element has a length which ranges from about 20 mm to about 35 mm and a circumference of about 17 mm to about 27 mm. The filter material can be any suitable material such as cellulose acetate, polypropylene, tobacco material, or the like. Filter materials having compositions or characteristics so as to exhibit low nicotine filtration efficiencies can be employed. The plug wrap typically is a conventional paper plug wrap, and can be either air permeable or essentially air impermeable. However, if desired, a nonwrapped cellulose acetate filter element can be employed. The various filter elements suitable for use in this invention can be manufactured using known cigarette filter making techniques and equipment.

Typically, the tipping material circumscribes the filter element and an adjacent region of the tobacco rod such that the tipping material extends about 3 mm to about 6 mm along the length of the tobacco rod. Typically, the tipping material is a conventional paper tipping material. The tipping material can have a porosity which can vary. For example, the tipping material can be essentially air impermeable, air permeable, or be treated (eg., by mechanical or laser perforation techniques) so as to have a region of perforations, openings or vents thereby providing a means for providing air dilution to the cigarette. The total surface area of the perforations and the positioning of the perforations along the periphery of the cigarette can be varied in order to control the performance characteristics of the cigarette.

As used herein, the term "air dilution" is the ratio (generally expressed as a percentage) of the volume of air drawn through the air dilution means to the total volume of air and aerosol drawn through the cigarette and exiting the extreme mouthend portion of the cigarette. For air diluted or ventilated cigarettes of this invention, the amount of air dilution can vary. Preferably, the amount of air dilution for a cigarette is greater than about 20 percent, more preferably greater than about 30 percent. The upper limit of air dilution for a cigarette typically is less than about 80 percent, more frequently less than about 60 percent.

The smokable material employed in the manufacture of the tobacco rod can vary. For example, the tobacco material can be engineered in a processed form such as an extruded form (eg., as a foamed extruded rod or extruded into a tubular shape), have the form of filler such as tobacco cut filler, or the like. Generally, the tobacco material of cigarettes has the form of cut filler. As used herein, the terms "filler" or "cut filler" are meant to include tobacco materials which have a form suitable for use in the manufacture of cigarette tobacco rods. As such, filler can include tobacco materials which are blended and are in a form ready for cigarette manufacture. The tobacco filler materials conveniently are employed in the form of strands or shreds as is common in conventional cigarette manufacture. For example, the tobacco cut filler material can be employed in the form of strands cut into widths ranging from about 1/25 inch to about 1/60 inch, preferably from about 1/30 inch to about 1/40 inch. Generally, such strands have lengths which range from about 0.25 inch to about 3 inches.

Tobacco materials can be cased and top dressed as is conventionally performed during various stages of cigarette manufacture. For example, additives such as flavorants and humectants can be applied to the tobacco material as is commonly done when cigarettes are manufactured. Suitable additives include flavorants such as vanillin, cocoa, licorice, menthol, tobacco aroma oils, tobacco extracts, and the like. Such additives conveniently are applied to the smokable material as top dressing components.

The majority of the filler material present in the smokable rod is a tobacco material. However, the tobacco material can be blended with another smokable material such as a tobacco substitute material. Examples of suitable tobacco materials include flue-cured, Burley, Maryland or Oriental tobaccos; processed tobacco materials such as expanded tobaccos, processed tobacco stems, reconstituted tobacco materials or reconstituted tobacco materials having varying levels of endogenous and exogenous nicotine; or blends thereof. If desired, the tobacco materials can be blended with small amounts of carbonized and/or pyrolyzed materials.

Tobacco material(s) having a naturally high nicotine content conveniently constitute at least a portion of the smokable filler material useful in manufacturing smoking articles of this invention. Typically, such useful high nicotine content tobaccos or high nicotine content processed tobaccos have nicotine contents of above about 2.5 percent. The nicotine contents of high nicotine tobacco materials oftentimes are above about 3 percent, frequently above about 4 percent, and in certain circumstances above about 5 percent. Generally, the nicotine content of tobacco materials useful in this invention does not exceed about 10 percent.

The high nicotine content filler material can vary. For example, tobaccos designated by the U.S.D.A. as Type 35 (One Sucker), Type 36 (Green River) or Type 37 (Virginia Sun Cured) are common tobaccos having a naturally high nicotine content. A cultivar such as *Nicotiana rustica* often has a natural nicotine content in the range of about 6 percent to about 10 percent. Additionally, also useful are upper stalk leaves of commercial lines of flue-cured tobacco (designated by the U.S.D.A. as Types 11-14) and Burley tobacco (designated by the U.S.D.A. as Type 31). The natural nicotine content of many tobaccos can depend upon the agronomic conditions under which the tobaccos are grown as well as the particular genetic line of the

tobacco.

Processed tobacco materials can be employed. Such processed tobaccos can be provided using tobacco reconstitution-type processes. For example, materials can be manufactured using extrusion, cast sheet, fourdrinier or paper making processes. Raw materials used in manufacturing processed tobaccos can include those high nicotine tobaccos described hereinbefore; or various types of tobacco extracts can be employed in the manufacturing steps of the processed tobaccos. Alternatively, processed tobaccos can be manufactured under conditions suitable to provide products having various nicotine levels. If desired, nicotine can be incorporated into the expansion solvents used to provide a volume expanded processed tobacco material having a high nicotine content. A typical expansion process is described in U.S. Patent No. 3,524,451 to Fredrickson. Also, processed tobacco materials include tobaccos or tobacco materials mixed, blended or otherwise treated with tobacco extracts, spray dried tobacco materials or tobacco aroma oils. As such, the processed tobacco materials have high nicotine contents upon completion of the processing steps involved in their preparation or manufacture, and prior to their use in the manufacture of cigarettes.

High nicotine tobacco(s) and/or high nicotine processed tobacco(s) can be employed as the tobacco material of the cigarette, as the component(s) of cigarette blends or as portions of the components of cigarette blends. For example, the high nicotine tobacco(s) and/or high nicotine processed tobacco material(s) can be blended with tobacco substitute(s) and/or tobacco material(s) having nicotine contents of less than about 2 percent. Typically, the so-called "American blends" having high nicotine contents (i.e., total blend nicotine contents above about 2 percent) are desirable for cigarette manufacture. Typical total nicotine contents of the tobacco material or blends of materials from which tobacco rods for cigarettes of this invention are manufactured are greater than about 2.25 percent, generally greater than 2.5 percent, often greater than about 3 percent, frequently greater than about 3.5 percent, and in certain circumstances greater than about 4 percent.

Organic acids useful herein are any organic acids or organic compounds that behave as Lewis acids when contacted with nicotine. Examples of organic acids useful in practicing the present invention are aromatic acids including benzoic-type acids and substituted benzoic-type acids, hydroxyacids, heterocyclic acids, terpenoid acids, sugar acids such as the pectic acids, amino acids, cycloaliphatic acids, dicarboxylic acids, aliphatic acids, keto acids, and the like. Preferred organic acids are the straight-chain and branched-chain aliphatic acids, more preferably the aliphatic monocarboxylic acids, and especially the keto aliphatic monocarboxylic acids. Examples of suitable organic acids include formic, acetic, propionic, isobutyric, butyric, alpha-methylbutyric, isovaleric, beta-methylvaleric, caproic, 2-furoic, phenylacetic, heptanoic, octanoic, nonanoic, malic, citric, oxalic, malonic, glycolic, succinic, ascorbic, tartaric, fumaric and pyruvic acids, as well as the lower fatty acids (i.e., having carbon chains less than C₁₂) and the higher fatty acids (i.e., having carbon chains of C₁₂ to C₂₀), and other such acids. The most preferred organic acid is a gamma keto aliphatic acid known as levulinic acid (CH₃COCH₂CH₂COOH). Levulinic acid also is known as acetylpropionic acid, alpha-ketovaleric acid and 4-oxypentanoic acid. Useful organic compounds which exhibit an acid character include the phenolics such as guaiacol, vanillin, protocatechualdehyde, and the like.

Numerous organic acids can improve the flavor or aroma of the aerosol, as numerous organic acids are suitable flavorants. However, whether a particular organic acid acts as a flavorant depends upon the amount of the particular organic acid employed as an additive as well as the flavor threshold of the particular acid employed. See, for example, *Tobacco Flavoring For Smoking Products*, by Leffingwell et al, p. 11 to 15 (1972). However, it may be desirable to use organic acids which provide specific flavor characteristics to the cigarette at low amounts in order to not provide undesirable off-tastes or aromas to the cigarette. For example, it may be desirable to employ certain organic acids at low enough levels in order that the cigarette does not exhibit taste or aroma characteristics which can be perceived as being chemical, metallic, bitter, pungent or soapy in nature, or as being dissonant to the general organoleptic characteristics associated with tobacco smoke.

The most preferred organic acid is levulinic acid. Such an organic acid can provide a smooth, palatable character to the cigarette while not providing any significant dissonant taste or aroma. If desired, certain amounts of various other organic acids can be blended with levulinic acid and employed as the additive of this invention. For example, it is desirable that a majority of the organic acid additive be levulinic acid.

The organic acid additive can be incorporated into the cigarette in a variety of places or sites. For example, the organic acid or organic acid mixture can be applied to the filler material, incorporated within some or all of the filler material, applied to the wrapper of the tobacco rod, applied within the glue line of the wrapper of the tobacco rod, provided within the filter element of the cigarette, or the like. If desired, the organic acid additive can be incorporated into processed tobaccos during the manufacture of such materials. For example, the organic acids can be mixed with tobacco extracts or tobacco aroma oils, and

the resulting tobacco material/organic acid mixture can be blended with, mixed with, or otherwise used to treat other tobacco(s) or tobacco material(s). The organic acid can be applied to the cigarette or be present within the cigarette in nondissociated form and/or in a dissociated (eg., carboxylate) form.

Typically, the organic acid additive is incorporated in the cigarette by admixing the additive with the tobacco material. The manner or process for applying the additive can vary depending upon whether the additive is applied diluted in liquid form, or upon the positioning of the additive within the cigarette. For example, the additive can be applied using syringes or techniques such as spraying, casing, electrostatic deposition, impregnation, garniture injection, spray drying, inclusion and encapsulation techniques, and the like.

Suitable solvents for the organic acids include water, ethanol, glycerol, propylene glycol, and the like, as well as combinations thereof.

One or more salts provided from nicotine and an organic acid can be incorporated into the cigarette. The use of such salts can provide for a cigarette having a relatively high nicotine content as well as provide the organic acid additive. Such salts can be incorporated into cigarettes which include tobacco materials having a wide range of nicotine contents.

Preferred nicotine/organic acid salts have a molar ratio of organic acid to nicotine of 1:1, 2:1 or 3:1, most preferably 3:1. The most preferred salts are totally ionized salts of nicotine and the organic acid. Such preferred ionized salts are those salts wherein both of the nicotine nitrogen atoms are ionized by the acid hydrogens of the organic acids. For example, a particularly preferred salt is provided from 1 mole of nicotine and 3 moles of levulinic acid and has a molar ratio thereof of 1:3.

The nicotine/organic acid salts conveniently are prepared using techniques generally known to those skilled in the art. Many of such techniques have been catalogued by Perfetti in Beitrag zur Tabakforschung International, Vol. 12, No. 2, p. 43 (1983), which is incorporated herein by reference. Preferably, nicotine/organic acid salts are provided by contacting nicotine with at least the stoichiometric amount of the organic acid necessary to form the particular salt under conditions sufficient to form the salt.

The preferred salts provided from nicotine and the organic acid generally are essentially non-volatile at conditions under which the smoking articles are manufactured and stored, however, specific properties of the various salts can vary. For example, nicotine/organic acid salts having straight-chain or branched-chain aliphatic acids having less than 20 carbon atoms generally have a molar ratio of 1:3 (nicotine:acid), and generally are liquid in form at ambient conditions. Such salts typically decompose at temperatures less than 100 °C, usually in the range from about 50 °C to about 60 °C. As another example, nicotine/organic acid salts having dicarboxylic organic acids generally have a molar ratio of 1:2 (nicotine:acid), and generally are solid in form at ambient conditions. Such salts typically decompose at temperatures in the range from about 90 °C to about 120 °C. As yet another example, nicotine/organic acid salts having acids containing phenyl groups generally have molar ratios of 1:1, 1:2 or 1:3 (nicotine:acid). Generally such salts are solid in form at ambient conditions. Such salts typically decompose at temperatures in the range from about 110 °C to about 200 °C.

Numerous nicotine/organic acid salts can improve the flavor or aroma of the aerosol, as numerous organic acids are suitable flavorants. Examples of salts which can provide flavor and aroma to the mainstream aerosol at certain levels include nicotine acetate, nicotine oxalate, nicotine malate, nicotine isovalerate, nicotine lactate, nicotine citrate, nicotine phenylacetate and nicotine myristate. However, it may be desirable to use salts which provide flavor characteristics to the cigarette at low amounts in order to not provide undesirable off-tastes or aromas to the cigarette.

The most preferred nicotine/organic acid salt is nicotine levulinate. Such a salt can provide a smooth, palatable character to the cigarette while not providing any significant dissonant taste or aroma. If desired, certain amounts of various nicotine/organic acid salts can be blended with nicotine levulinate and employed as the additive to provide cigarettes of this invention.

The salts can be incorporated into the cigarette in a variety of places or sites. For example, the salt can be applied to the filler material, incorporated within some or all of the filler material, applied to the wrapper of the tobacco rod, applied within the glue line of the wrapper of the tobacco rod, applied within a region (eg., a cavity) which is subjected to heat, or the like.

Typically, the nicotine/organic acid salt additive or additive mixture is incorporated in the cigarette by admixing the additive with the tobacco material. The manner or process for applying the additive can vary depending upon whether the additive is applied in solid or liquid form, or upon the positioning of the additive within the cigarette. For example, the additive can be applied using syringes or techniques such as spraying, electrostatic deposition, impregnation, garniture injection, spray drying, inclusion and encapsulation techniques, and the like.

When the nicotine/organic acid salts are applied using spraying techniques it is desirable to form a liquid solution of the salt in a suitable solvent. Such solutions should exhibit a low enough viscosity to allow for spraying or injecting the solution. However, it is desirable that the concentration of the salt within the solution not be so dilute that the salt experiences significant dissociation. Typically, the concentration of salt within the solution is about 20 weight percent or more.

Suitable solvents for the salts include water, ethanol, glycerol, propylene glycol, and the like, as well as combinations thereof. Generally, most nicotine/organic acid salts are soluble or miscible in such solvents, and the salts do not undergo substantial dissociation when solubilized to small amounts. For example, the salt can be hydrated in water without undergoing a significant amount of dissociation. However, salts diluted with substantial amounts of solvent can undergo dissociation to some degree to provide for the application of a mixture of nicotine/organic acid salt, nicotine and organic acid to the cigarette. Thus, it is possible to apply an additive in the form of nicotine and levulinic acid to the cigarette.

If desired, cigarettes can have incorporated therein as an additive (i) at least one salt consisting of nicotine and an organic acid, and (ii) nicotine. Preferred additives of such type include at least one salt having a molar ratio of nicotine to organic acid of 1:3.

The amount of organic acid employed within the cigarette can vary. The amount of organic acid incorporated within the cigarette depends upon factors such as the placement of the organic acid within the cigarette, and the configurational aspects of the cigarette. Configurational aspects include the composition and characteristics of the filter material and initial filler blend, the degree of ventilation of the cigarette, and other such factors. For example, for most cigarettes of this invention comprising tobacco material having a total or blend nicotine content of from about 2 percent to about 10 percent, it frequently is desirable to provide organic acid additive to the cigarette in an amount from about 1 percent to about 10 percent, based on the dry weight of the tobacco filler material in order to provide acceptable tobacco taste, strength and satisfaction upon use. Generally, the amount of organic acid applied to such a cigarette is greater than about 2 percent, and oftentimes greater than about 3 percent, based on the dry weight of the tobacco filler material within the cigarette.

The amount of nicotine/organic acid salt or salts employed within the cigarette can vary. The amount of salt incorporated within the cigarette depends upon factors such as the placement of the salt within the cigarette, and the configurational aspects of the cigarette. For most cigarettes having tobacco filler material comprising a nicotine content of from about 1 percent to about 2 percent, it frequently is desirable to provide salt additive to provide a total nicotine content of up to about 8 percent, more frequently up to about 4 percent to the cigarette. Such an amount of additive can provide for good tobacco taste, strength and satisfaction upon use. Generally, the amount of nicotine/organic acid salt applied to a typical cigarette provides from about 0.25 percent to about 20 percent, preferably from about 1.2 to about 13 percent of salt additive, based on the dry weight of the tobacco filler material within that cigarette. In certain instances, it is desirable to employ about 3.5 percent of salt additive or more, based on the dry weight of the tobacco filler material within the cigarette.

The cigarettes of this invention preferably provide a mainstream aerosol exhibiting a pH which is essentially equal to or less than that of a similar cigarette having a low amount (e.g., less than about 0.2 weight percent) of the organic acid additive incorporated therein. In certain circumstances, an amount of organic acid additive is incorporated into a cigarette in order to reduce the pH of the mainstream aerosol during use thereof. Mainstream aerosol is that aerosol which is drawn through the article and into the mouth of the user. For example, for a cigarette having smokable tobacco material contained in a circumscribing outer wrapping material, the mainstream aerosol is the mainstream tobacco smoke which includes the combustion and/or pyrolysis products of tobacco material.

By the term, "pH of mainstream aerosol" is meant that averaged per-inhalation pH of the whole aerosol as measured using the techniques described by Sensabaugh et al in Tobacco Science, Vol. XI, pp. 25-30 (1967), which is incorporated herein by reference. Typical mainstream aerosol pH for a cigarette ranges from about 4.5 units to about 8.5 units on average per cigarette.

In referring to a reduction in the pH of mainstream aerosol, it is meant a lowering of the average pH of the mainstream aerosol per particular cigarette. Such reduction is provided by the addition of an effective amount of the additive (e.g., organic acid additive and/or nicotine/organic acid salt). Typically, the reduction in pH is a lowering of the pH by more than about 0.03 pH unit; preferably by more than about 0.08 pH unit. Typically, reduction in the pH of the mainstream aerosol does not provide a cigarette which yields mainstream aerosol having a pH significantly below 4.5 units.

The presence of the organic acid (which can be provided by the decomposition of the nicotine/organic acid salt during use of the cigarette can introduce a reduction of the pH of the mainstream aerosol depending upon the quantity and type of organic acid which is incorporated therein. Thus, a certain

balance, mellowing or marrying of the flavors culminate in a fuller bodied tobacco flavor, strength and satisfaction which is delivered to the user. Such a flavor enhancing characteristic is particularly desirable for highly air diluted or "ultra low tar" cigarettes.

The pH of the mainstream aerosol is influenced by a number of factors. For example, the pH of mainstream cigarette smoke can be influenced by factors such as the type of tobacco material or blend of tobacco materials employed, the type of processed tobacco (eg., volume expanded tobacco or reconstituted tobacco), the configuration of the cigarette (eg., the filter tow material, the degree of air dilution, the circumference of the cigarette, the type of wrapping material, etc.), the manner of drawing on or puffing the cigarette, and other such factors.

Cigarettes of this invention generally deliver from about 0.2 mg to about 3.5 mg, frequently from about 0.3 mg to about 2.5 mg, more frequently from about 0.4 mg to about 1.5 mg of nicotine when smoked under FTC conditions. Typically, FTC "tar" to FTC nicotine ratios for cigarettes of this invention are less than about 12, generally less than about 9, frequently less than about 7, and in certain instances less than about 5. FTC "tar" to FTC nicotine ratios for cigarettes of this invention often can range from about 3 to about 6. Typically, the FTC "tar" to FTC nicotine ratios of a cigarette having a nicotine/organic acid salt incorporated therein can be lowered by up to about 80 percent of that ratio of similar cigarette not having the salt additive incorporated therein.

The following examples are provided in order to further illustrate the invention but should not be construed as limiting the scope thereof. Unless otherwise noted, all parts and percentages are by weight.

EXAMPLE 1

A salt of nicotine and levulinic acid is provided using the following procedure.

Into a 1,000 ml round bottom flask is charged about 350 g of 1-nicotine provided from Kodak Laboratory Chemicals, Eastman Kodak Co. (Catalogue No. 52, p. 366, Chemical No. 1124973). To the 1-nicotine is charged about 10 g of sodium hydroxide pellets. The flask is fitted with a heating mantle and equipped with a magnetic stirring bar. The nicotine solution is stirred employing a magnetic stirring unit. The nicotine is vacuum distilled using a Todd Column packed with glass helixes, and the fraction distilled between 97°C and 98°C at 10 mm Hg pressure is collected at a reflux ratio of about 10:1. The collected distillate is water clear. The nicotine so purified using the vacuum distillation technique is employed in the preparation of the 1-nicotine/levulinic acid salt.

Into a 500 ml round bottom flask equipped with a magnetic stirring bar and heating mantle is charged 69.6 g (0.6 mole) of levulinic acid. The levulinic acid is stripped employing a conventional magnetic stirring unit. The levulinic acid is obtained from Aldrich Chemical Co., Catalogue No. 1984-85, p. 672, Compound No. L-200-9, and is employed without further purification. The levulinic acid is heated to about 50°C in order to provide a liquid form thereof, and the liquified component is subjected to stirring. To the liquified levulinic acid is titrated 32.4 g (0.2 mole) of the purified 1-nicotine over about a 20 minute time period. It is preferred to introduce the nicotine to the organic acid in order to provide an environment of excess acid to nicotine and thus promote the formation of salt. A clear, viscous yellow colored material weighing about 100 g results. The product is sealed in a glass ampoule under nitrogen.

The product is 1-nicotine levulinate (as determined using infrared spectrometry), and has a nicotine to levulinic acid ratio of 1:3 (as determined by a destructive distillation in a 10 percent sodium hydroxide aqueous solution, subsequent extraction using isopropanol, and gas chromatographic analysis for nicotine). The salt is believed to have a structure substantially as generally described in Fig. 13 of the Perfetti reference, supra.

Cigarettes incorporating varying amounts of the 1-nicotine levulinate salt are provided using the following procedure.

Cigarettes having lengths of about 99 mm and circumferences of about 24.85 mm have tobacco rod lengths of 68 mm and filter element lengths of 31 mm. The tobacco rod includes a charge of tobacco cut filler weighing about 0.74 g contained in a circumscribing cigarette paper wrap which is sold commercially as 754 Cigarette Paper by Ecusta Corp. The filter element is manufactured using conventional cigarette filter making technology from cellulose acetate tow (2.7 denier per filament, 48,000 total denier) and circumscribing air permeable paper plug wrap having a CORESTA porosity of 26,000 cm/min. The tobacco rod and filter element are aligned in an abutting, end-to-end relationship and secured together using tipping paper having a CORESTA porosity of 3135 ml/min. The tipping paper is adhesively secured to the filter element and the adjacent portion of the tobacco rod. The tipping material circumscribes the length of the filter element and about 3 mm of the length of the tobacco rod. Cigarettes so described are manufactured using a Pilot Cigarette Maker from Hauni-Werke Korber & Co. KG. A ring of mechanically provided

perforations extends around the periphery of the cigarette about 13 mm from the extreme mouthend thereof. The perforations so provided yield cigarettes which are 50 percent air diluted. The cigarettes so manufactured are designated Sample Nos. 1, 2, 3 and C-1, corresponding to the sample of filler material from which each cigarette is manufactured.

5 The filler material employed in providing the tobacco rod is in the form of strands cut at about 32 cuts per inch. The initial filler material includes a blend of about 9 percent Burley tobacco, about 41 percent flue-cured tobacco, about 32 percent reconstituted tobacco material, and about 18 percent Oriental tobaccos. The blend has an aqueous casing of glycerin and flavors applied thereto.

10 Four lots of the cut filler blend, each lot weighing 1,520 g, are provided. The first lot is treated with 20 g of the 1-nicotine levulinate additive. The second lot is treated with 60 g of the 1-nicotine levulinate additive. The third lot is treated with 100 g of the 1-nicotine levulinate additive. The fourth lot is not treated with the 1-nicotine levulinate additive and is employed for comparison purposes.

The 1-nicotine levulinate additive is applied to cut filler as a spray using a hand sprayer to apply a 1:1 mixture of water and additive.

15 Each of the four lots are separately placed in sealed plastic bags and stored at 70 °F for 2 days. Then, the four lots are each mixed with about 480 g of a cut filler mixture of about 75 parts volume expanded Burley tobacco and about 25 parts volume expanded flue-cured tobacco. The volume expanded cut filler mixture is added to each lot using a mixing drum in order to provide a well mixed blend having a moisture content of about 12 percent to about 13 percent. The resulting blend provided from the first lot of filler material has about 1 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 1. The resulting blend provided from the second lot of filler material has about 3 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 2. The resulting blend provided from the third lot of filler material has about 5 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 3. The resulting blend provided from the fourth lot of filler material is not treated with the 1-nicotine levulinate salt additive, is employed for comparison purposes, and is designated as Sample No. C-1.

20 The various cigarettes are smoked under FTC conditions. Data concerning (i) FTC "tar," FTC nicotine and FTC carbon monoxide, (ii) the "tar"/nicotine ratio, (iii) cigarette nicotine content, (iv) puff count, and (v) pH of the mainstream aerosol for each sample are presented in Table I.

35

40

45

50

55

TABLE I

Sample	FTC "tar" (mg/cigarette) ¹	FTC Nicotine ¹ (mg/cigarette)	FTC CO (mg/cigarette) ¹	"Tar"/ ² Nicotine	Total Nicotine (%) ³	Puff Count ⁴	Smoke pH ⁵	
							minimum	maximum
1	5.1	0.56	7.4	9.1	2.05	8.7	5.75	6.01
2	4.9	0.69	7.4	7.1	2.51	8.9	5.65	6.02
3	4.9	0.81	6.7	6.0	2.91	9.0	5.67	5.98
C-1*	4.6	0.38	7.5	12.1	1.66	8.8	5.85	6.10

*Not an example of the invention.

1. FTC conditions consist of two seconds of puffing (35 ml total volume) separated by 58 seconds of smolder.
2. "Tar"/nicotine is the ratio of FTC "tar" to FTC nicotine delivered by the cigarette.
3. Total nicotine is the total amount of nicotine (i.e., as nicotine present within the cigarette from all sources and based on the dry weight of the filler). See, the Harvey et al reference, supra.
4. Puff count is the average number of puffs per cigarette provided under FTC smoking conditions.
5. Smoke pH is determined using the techniques described in the Sensabaugh et al reference, supra. The presented minimum and maximum pH value for each cigarette are the calculated average of per-puff minimum and maximum values obtained for 8 puffs per cigarette.

The data in Table I indicate that the various cigarettes have increased nicotine contents and exhibit increased FTC nicotine values as the level of 1-nicotine levulinate is increased. In addition, the FTC "tar" to nicotine ratios for the samples decrease as the level of 1-nicotine levulinate is increased. The various cigarettes each exhibit similar "tar" deliveries, carbon monoxide deliveries and puff counts. Further, the samples of the invention (i.e., Sample Nos. 1-3) exhibit a pH of the whole smoke lower than that of the

sample not having the exogenous nicotine/organic acid salt (i.e., Sample No. C-1).

Evaluations of the organoleptic properties of the Sample Nos. 2, 3 and C-1 indicate that the cigarette having about 5 percent salt additive (i.e., Sample No. 3) exhibits greater impact and smoothness as well as less harshness than the cigarette not having salt additive (i.e., Sample No. C-1). Sample No. 2 is not significantly different organoleptically from Sample No. C-1 in terms of harshness and overall taste, even through there is a substantial increase in FTC nicotine of the sample relative to the comparative sample. Thus, the nicotine levulinate additive provides for a cigarette having a relatively low FTC "tar" to FTC nicotine ratio while having a smooth (i.e., not overly harsh) taste.

10 EXAMPLE 2

Cigarettes incorporating varying amounts of the 1-nicotine levulinate salt are provided using the following procedure.

Cigarettes having lengths of about 84 mm and circumferences of about 24.85 mm have tobacco rod lengths of 57 mm and filter element lengths of 27 mm. The tobacco rod includes a charge of tobacco cut filler weighing about 0.49 g contained in a circumscribing cigarette paper wrap which is sold commercially as 854 Cigarette Paper by Ecusta Corp. The filter element is manufactured using conventional cigarette filter making technology from cellulose acetate tow (2.1 denier per filament, 48,000 total denier) and circumscribing non-air permeable paper plug wrap. The tobacco rod and filter element are aligned in an abutting, end-to-end relationship and secured together using a non-air permeable tipping paper. The tipping paper is adhesively secured to the filter element and the adjacent portion of the tobacco rod. The tipping material circumscribes the length of the filter element and about 3 mm of the length of the tobacco rod. Cigarettes so described are manufactured using a Pilot Cigarette Maker from Hauni-Werke Korber & Co. KG. A ring of laser perforations are provided around the periphery of the cigarette about 13 mm from the extreme mouthend thereof. The perforations penetrate through the tipping paper and plug wrap, and are provided using a Laboratory Laser Perforator from Hauni-Werke Korber & Co. KG. The perforated cigarette is 75 percent air diluted. The cigarettes so manufactured are designated Sample Nos. 4, 5, 6 and C-2, corresponding to the sample of filler material from which each cigarette is manufactured.

The filler material employed in providing the tobacco rod is in the form of strands cut at about 32 cuts per inch. The initial filler material includes a blend of about 43 percent burley tobacco, about 6 percent flue-cured tobacco, about 19 percent reconstituted tobacco material, and about 32 percent Turkish tobacco. The blend has an aqueous casing of glycerin and flavors applied thereto.

Four lots of the cut filler blend, each lot weighing 940 g, are provided. The first lot is treated with 60 g of the 1-nicotine levulinate additive. The second lot is treated with 140 g of the 1-nicotine levulinate additive. The third lot is treated with 200 g of the 1-nicotine levulinate additive. The fourth lot is not treated with the 1-nicotine levulinate additive and is employed for comparison purposes.

The 1-nicotine levulinate additive is applied to cut filler as a spray using a hand sprayer to apply a 1:1 mixture of water and additive.

Each of the four lots are separately placed in sealed plastic bags and stored at 70 °F for 2 days. Then, the four lots are each mixed with about 1,060 g of a cut filler mixture of about 35 parts volume expanded burley tobacco and about 65 parts volume expanded flue-cured tobacco. The volume expanded cut filler mixture is added to each lot using a mixing drum in order to provide a well mixed blend having a moisture content of about 12 percent to about 13 percent. The resulting blend provided from the first lot of filler material has about 3 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 4. The resulting blend provided from the second lot of filler material has about 7 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 5. The resulting blend provided from the third lot of filler material has about 10 percent of the 1-nicotine levulinate salt applied thereto (based on the filler conditioned weight) and is designated as Sample No. 6. The resulting blend provided from the fourth lot of filler material is not treated with the 1-nicotine levulinate salt additive, is employed for comparison purposes, and is designated as Sample No. C-2.

For comparison purposes, Sample No. C-3 is prepared. Sample No. C-3 is provided by adding nicotine to a cigarette designated as Sample No. C-2. In particular, about 30 mg of a 1:1 mixture of ethanol and 85 percent pure 1-nicotine is injected into the cigarette in order to provide a nicotine content of about 3.92 percent to the cigarette. The nicotine/ethanol mixture is incorporated into the tobacco rod by inserting a syringe into the lighting end of the rod and slowly pulling the syringe from the rod while injecting the mixture into the rod.

Sample No. 7 is provided by injecting about 10 mg of the previously described 1:1 mixture of ethanol nicotine into a cigarette designated as Sample No. 6 using a syringe in the manner previously described. The cigarette so provided comprises a nicotine levulinate additive as well as an exogenous nicotine additive.

5 The various cigarettes are smoked under FTC conditions. Data concerning (i) FTC "tar," FTC nicotine and FTC carbon monoxide, (ii) the "tar"/nicotine ratio, (iii) cigarette nicotine content, and (iv) puff count for Sample Nos. 4-6 and C-2 are presented in Table II. In addition, data concerning the pH of the mainstream aerosol for Sample Nos. 4-6, C-2 and C-3 are presented in Table II.

10

15

20

25

30

35

40

45

50

55

TABLE II

Sample	FTC "tar" (mg/cigarette) ¹	FTC Nicotine (mg/cigarette) ¹	FTC CO (mg/cigarette) ¹	"Tar"/ Nicotine ²	Total Nicotine (%) ³	Puff ⁴ Count	Smoke pH ⁵ minimum maximum
4	1.8	0.29	2.9	6.2	2.64	6.7	5.90 6.28
5	2.0	0.39	3.0	5.1	3.22	6.8	5.86 6.20
6	2.0	0.51	3.1	3.9	3.92	6.8	5.91 6.32
C-2*	1.8	0.18	2.9	10.0	2.08	6.7	6.13 6.42
C-3*	—	—	—	—	—	—	6.78 7.11

*Not an example of the invention.

1-4 - See Table I, footnotes 1-4, respectively.

5. Smoke pH is determined using the techniques described in the Sensabaugh et al reference, supra. The presented minimum and maximum pH value for each cigarette are the calculated average of per-puff minimum and maximum values obtained for a number of puffs per cigarette. For Sample Nos. 4, 5 and C-2, the number of puffs used to calculate the average pH values is 7. For Sample Nos. 6 and C-3, the number of puffs used to calculate the average pH values is 6.

The data in Table II indicate that the various cigarettes have increased nicotine contents and exhibit increased FTC nicotine values as the level of 1-nicotine levulinate is increased. In addition, the FTC "tar" to nicotine ratios for the samples decrease as the level of 1-nicotine levulinate is increased. The various cigarettes each exhibit similar "tar" deliveries, carbon monoxide deliveries and puff counts. Further, the samples of the invention (i.e., Sample Nos. 4-6) exhibit a pH of the whole smoke lower than that of the

sample not having the exogenous nicotine/organic acid salt (i.e., Sample No. C-2). In addition, the pH of the whole smoke of Sample No. C-3 is very much higher than that of any of the other samples.

Evaluations of the organoleptic properties of Sample Nos. 5, 6 and C-2 indicate that the cigarette having about 10 percent salt additive (i.e., Sample No. 6) exhibits greater impact and smoothness as well as less harshness than the cigarette not having the salt additive (i.e., Sample No. C-2). All cigarettes sampled provide good tobacco taste and do not exhibit a perceivable chemical off-taste or non-cigarette taste. Surprisingly, Sample No. 5 is not significantly different organoleptically from Sample No. C-2 in terms of impact, smoothness, harshness and overall taste even though the sample provides a higher level of FTC nicotine than the comparative sample. Sample No. C-3 is extremely harsh and is not palatable. However, Sample No. 7 surprisingly exhibits a smooth smoking character and is palatable, even though the sample has a relatively high level of exogenous nicotine incorporated therein.

EXAMPLE 3

Cigarettes having a high nicotine content and incorporating varying amounts of the levulinic acid are provided using the following procedure.

Cigarettes having lengths of about 84 mm and circumferences of about 24.85 mm have tobacco rod lengths of 57 mm and filter element lengths of 27 mm. The tobacco rod includes a charge of tobacco cut filler weighing about 0.76 g contained in a circumscribing cigarette paper wrap which is sold commercially as 854 Cigarette Paper by Ecusta Corp. The filter element is manufactured using conventional cigarette filter making technology from cellulose acetate tow (2.1 denier per filament, 48,000 total denier) and circumscribing air permeable paper plug wrap having a CORESTA porosity of 26,000 cm/min. The tobacco rod and filter element are aligned in an abutting, end-to-end relationship and secured together using porous (air permeable) tipping paper. The tipping paper is adhesively secured to the filter element and the adjacent portion of the tobacco rod. The tipping material circumscribes the length of the filter element and about 4 mm of the length of the tobacco rod. Cigarettes so described are manufactured using a Pilot Cigarette Maker from Hauni-Werke Korber & Co. KG. A ring of mechanically provided perforations extends around the periphery of the cigarette about 13 mm from the extreme mouthend thereof. The perforations so provided yield cigarettes which are 75 percent air diluted. The cigarettes so manufactured are designated Sample Nos. 8, 9, 10 and C-4, corresponding to the sample of filler material from which each cigarette is manufactured.

The filler material employed in providing the tobacco rod is in the form of strands cut at about 32 cuts per inch. The initial filler material includes a blend of about 40 percent Burley tobacco having a nicotine content of about 5 percent, about 18 percent flue-cured tobacco having a nicotine content of about 3.5 percent, about 30 percent reconstituted tobacco material having a nicotine content of about 0.5 percent, and 12 percent of an Oriental tobacco blend having a nicotine content of about 0.9 percent. The blend has an aqueous casing of glycerin and flavors applied thereto.

Four lots of the cut filler blend, each lot weighing 2,000 g on a dry weight basis, are provided. The first lot is treated with 120 g of the levulinic acid additive. The second lot is treated with 280 g of the levulinic acid additive. The third lot is treated with 400 g of the levulinic acid additive. The fourth lot is not treated with the levulinic acid additive and is employed for comparison purposes.

The levulinic acid additive is applied to cut filler as a spray using a hand sprayer as a mixture of water and additive. The quantity of water of the water/additive mixture is adjusted to attain a final cut filler moisture content of about 15 percent.

Each of the four lots are separately placed in sealed plastic bags and stored at 70 °F for 2 days. Then, the four lots are each mixed with about 2,000 g on a dry weight basis, of a cut filler mixture of about 35 parts volume expanded Burley tobacco having a nicotine content of about 4 percent, and about 65 parts volume expanded flue-cured tobacco having a nicotine content of about 4 percent. The volume expanded cut filler mixture is added to each lot using a mixing drum in order to provide a well mixed blend having a moisture content of between about 12 percent and about 13 percent.

The resulting blend provided from the first lot of filler material has about 3 percent of the levulinic acid applied thereto (based on the filler dry weight) and is designated as Sample No. 8. The resulting blend provided from the second lot of filler material has about 7 percent of the levulinic acid applied thereto (based on the filler dry weight) and is designated as Sample No. 9. The resulting blend provided from the third lot of filler material has about 10 percent of the levulinic acid applied thereto (based on the filler dry weight) and is designated as Sample No. 10. The resulting blend provided from the fourth lot of filler material is not treated with the levulinic acid additive, is employed for comparison purposes, and is designated as Sample No. C-4.

The various cigarettes are smoked under FTC conditions. Data concerning (i) the nicotine content of each blend, (ii) FTC "tar," FTC nicotine and FTC carbon monoxide, (iii) the "tar"/nicotine ratio, (iv) puff count, and (v) pH of the mainstream aerosol for each sample, are presented in Table III.

TABLE III

<u>Sample</u>	<u>FTC "Tar"¹</u> <u>(mg/cigarette)</u>	<u>FTC Nicotine¹</u> <u>(mg/cigarette)</u>	<u>FTC CO¹</u> <u>(mg/cigarette)</u>	<u>"Tar"/²</u> <u>Nicotine</u>	<u>Total³</u> <u>Nicotine (%)</u>	<u>Puff⁴</u> <u>Count</u>	<u>Smoke pH⁵</u>		<u>Average⁶</u> <u>Smoke pH</u>
							<u>minimum</u>	<u>maximum</u>	
8	1.2	0.27	2.08	5.22	3.12	6.7	6.12	6.41	6.57
9	1.4	0.23	2.10	6.09	3.00	6.7	6.16	6.30	6.16
10	1.5	0.23	2.18	5.56	2.94	6.8	5.48	5.82	5.20
C-4*	1.2	0.21	2.04	5.71	3.08	6.7	6.47	6.82	6.79

*Not an example of the invention.

1-4 - See Table I, footnotes 1-4, respectively.

5. Smoke pH is determined using the techniques described in the Sensabaugh et al reference, supra. The presented minimum and maximum pH value for each cigarette are the calculated average of per-puff minimum and maximum values obtained for 7 puffs per cigarette.
6. Average smoke pH is the "twenty port" smoke pH for the mainstream smoke of 20 cigarettes as determined using techniques described by Harris et al, 32nd Tob. Chem. Res. Conf., (1978).

The data in Table III indicate that the various cigarettes having high nicotine content cut filler (i.e., approximately 3 percent total blend nicotine) exhibit comparable FTC "tar," nicotine and carbon monoxide deliveries, as well as comparable FTC "tar" to FTC nicotine ratios and puff counts. However, cigarettes of the invention (i.e., Sample Nos. 8-10 which contain the levulinic acid additive) exhibit reduced mainstream by puff and average smoke pH when compared to a control (i.e., Sample No. C-4 which does not have the levulinic acid additive). In addition, the data indicate that the smoke pH of cigarettes of the invention is reduced significantly as the level of levulinic acid additive increases. The reduction in the smoke pH of the samples of the invention is indicative of a substantial increase in the hydronium ion concentration of the tobacco smoke. Such an increase in the hydronium ion concentration of the mainstream smoke is sufficient to provide a change in the organoleptic quality of the smoke.

Organoleptic evaluation of the samples indicates that the cigarettes of the invention are smooth smoking while the control sample is very harsh. The mildness of Sample Nos. 8 and 9 is considered comparable. The cigarettes of the invention yield good tobacco taste, strength and smoking satisfaction. The control sample is very strong, and the overpowering sensation provided thereby is not satisfying.

EXAMPLE 4

Cigarettes incorporating varying amounts of the levulinic acid are provided using the following procedure.

Cigarettes having lengths of about 84 mm and circumferences of about 24.85 mm have tobacco rod lengths of 57 mm and filter element lengths of 27 mm. The tobacco rod includes a charge of tobacco cut filler weighing about 0.82 g contained in a circumscribing cigarette paper wrap which is sold commercially as 856 Cigarette Paper by Ecusta Corp. The filter element is manufactured using conventional cigarette filter making technology from cellulose acetate tow (2.7 denier per filament, 48,000 total denier) and circumscribing air permeable paper plug wrap having a CORESTA porosity of about 26,000 cm/min. The tobacco rod and filter element are aligned in an abutting, end-to-end relationship and secured together using essentially air impermeable tipping paper. The tipping paper is adhesively secured to the filter element and the adjacent portion of the tobacco rod. The tipping material circumscribes the length of the filter element and about 4 mm of the length of the tobacco rod. Cigarettes so described are manufactured using a Pilot Cigarette Maker from Hauni-Werke Korber & Co. KG. A ring of laser perforations extends around the periphery of the cigarette about 13 mm from the extreme mouthend thereof. The perforations so provided yield cigarettes which are 50 percent air diluted. The cigarettes so manufactured are designated Sample Nos. 11, 12, 13 and C-5, corresponding to the sample of filler material from which each cigarette is manufactured.

The filler material employed in providing the tobacco rod is in the form of strands cut at about 32 cuts per inch. The initial filler material includes a blend of about 31 percent Burley tobacco having a nicotine content of about 5 percent, about 20 percent flue-cured tobacco having a nicotine content of about 3.5 percent, about 31 percent reconstituted tobacco material having a nicotine content of about 0.5 percent, and 18 percent of an Oriental tobacco blend having a nicotine content of about 0.9 percent. The blend has an aqueous casing of glycerin and flavors applied thereto.

Four lots of the cut filler blend, each lot weighing 3,120 g on a dry weight basis, are provided. The first lot is treated with 40 g of the levulinic acid additive. The second lot is treated with 120 g of the levulinic acid additive. The third lot is treated with 200 g of the levulinic acid additive. The fourth lot is not treated with the levulinic acid additive and is employed for comparison purposes.

The levulinic acid additive is applied to cut filler as a spray using a hand sprayer as a mixture of water and additive. The quantity of water of the water/additive mixture is adjusted to attain a final cut filler moisture content of about 15 percent.

Each of the four lots are separately placed in sealed plastic bags and stored at 70 °F for 2 days. Then, the four lots are each mixed with about 880 g on a dry weight basis, of a cut filler mixture of about 35 parts volume expanded Burley tobacco having a nicotine content of about 4 percent, and about 65 parts volume expanded flue-cured tobacco having a nicotine content of about 4 percent. The volume expanded cut filler mixture is added to each lot using a mixing drum in order to provide a well mixed blend having a moisture content of between about 12 percent and about 13 percent.

The resulting blend provided from the first lot of filler material has about 1 percent of the levulinic acid applied thereto (based on the filler dry weight) and is designated as Sample No. 11. The resulting blend provided from the second lot of filler material has about 3 percent of the levulinic acid applied thereto (based on the filler dry weight) and is designated as Sample No. 12. The resulting blend provided from the third lot of filler material has about 5 percent of the levulinic acid applied thereto (based on the filler dry

weight) and is designated as Sample No. 13. The resulting blend provided from the fourth lot of filler material is not treated with the levulinic acid additive, is employed for comparison purposes, and is designated as Sample No. C-5.

5 The various cigarettes are smoked under FTC conditions. Data concerning (i) the nicotine content of each blend, (ii) FTC "tar," FTC nicotine and FTC carbon monoxide, (iii) the "tar"/ nicotine ratio, (iv) puff count, and (v) pH of the mainstream aerosol for each sample, are presented in Table IV.

10

15

20

25

30

35

40

45

50

55

TABLE IV

Sample	FTC "Tar" ¹ (mg/cigarette)	FTC Nicotine ¹ (mg/cigarette)	FTC CO ¹ (mg/cigarette)	"Tar" ² / Nicotine	Total ³ Nicotine (%)	Puff ⁴ Count	Smoke pH ⁵ minimum maximum	Average ⁶ Smoke pH
11	5.2	0.54	6.95	9.63	2.55	6.0	6.25 6.57	6.43
12	4.9	0.56	6.53	8.75	2.64	5.9	6.35 6.75	6.28
13	5.1	0.60	6.53	8.50	2.58	6.0	5.69 5.97	5.56
C-5*	5.0	0.58	6.87	8.62	2.44	6.0	6.47 6.80	6.61

*Not an example of the invention.

1-4 - See Table I, footnotes 1-4, respectively.

5. Smoke pH is determined using the techniques described in the Sensabaugh et al reference, *supra*. The presented minimum and maximum pH value for each cigarette are the calculated average of per-puff minimum and maximum values obtained for 7 puffs per cigarette.

6. Average smoke pH is the "twenty port" smoke pH for the mainstream smoke of 20 cigarettes as determined using techniques described by Harris et al, *supra*.

The data in Table IV indicate that the various cigarettes of this invention having high nicotine content cut filler (i.e., more than 2.5 percent total blend nicotine) exhibit FTC "tar," nicotine and carbon monoxide deliveries comparable to the control cigarette. The various cigarettes also exhibit comparable FTC "tar" to nicotine ratios and puff counts. However, cigarettes of the invention (i.e., Sample Nos. 11-13 which contain levulinic acid additive) exhibit reduced mainstream by puff and average smoke pH when compared to a

control (i.e., Sample No. C-5 which does not have the levulinic acid additive).

Organoleptic evaluation of the samples indicates that the cigarettes of the invention are smooth smoking while the control sample is very harsh. The mildness of Sample Nos. 12 and 13 is considered comparable. The cigarettes of the invention yield good tobacco taste, strength and smoking satisfaction. The control sample is very strong, and the overpowering sensation provided thereby is not satisfying.

EXAMPLE 5

Cigarettes incorporating varying amounts of the levulinic acid are provided using the following procedure.

Cigarettes having lengths of about 84 mm and circumferences of about 24.85 mm have tobacco rod lengths of 57 mm and filter element lengths of 27 mm. The tobacco rod includes a charge of tobacco cut filler weighing about 0.82 g contained in a circumscribing cigarette paper wrap which is sold commercially as 856 Cigarette Paper by Ecusta Corp. The filter element is manufactured using conventional cigarette filter making technology from cellulose acetate tow (2.7 denier per filament, 48,000 total denier) and circumscribing air permeable paper plug wrap having a CORESTA porosity of about 26,000 cm/min. The tobacco rod and filter element are aligned in an abutting, end-to-end relationship and secured together using essentially air impermeable tipping paper. The tipping paper is adhesively secured to the filter element and the adjacent portion of the tobacco rod. The tipping material circumscribes the length of the filter element and about 4 mm of the length of the tobacco rod. Cigarettes so described are manufactured using a Pilot Cigarette Maker from Hauni-Werke Korber & Co. KG. The cigarettes so manufactured are designated Sample Nos. 14, 15, 16 and C-6, corresponding to the sample of filler material from which each cigarette is manufactured.

The filler materials employed in providing the tobacco rods for Sample Nos. 14, 15, 16 and C-6 are the filler materials described for Sample Nos. 11, 12, 13 and C-5, respectively.

The various cigarettes are smoked under FTC conditions. Data concerning (i) the nicotine content of each blend, (ii) FTC "tar" and FTC nicotine, (iii) the "tar"/nicotine ratio, (iv) puff count, and (v) pH of the mainstream aerosol for each sample, are presented in Table V.

TABLE V

Sample	FTC "Tar" ¹ (mg/cigarette)	FTC Nicotine ¹ (mg/cigarette)	"Tar" ² Nicotine	Total ³ Nicotine (t)	Puff ⁴ Count	Average ⁵ Smoke pH
14	9.3	0.87	10.7	2.55	7.1	6.36
15	9.4	0.91	10.3	2.64	7.0	5.56
16	11.0	1.06	10.4	2.58	7.0	5.56
C-6*	9.6	0.86	11.2	2.44	7.1	6.54

*Not an example of the invention.

1-4 - See Table I, footnotes 1-4, respectively.

5. Average smoke pH is the "twenty port" smoke pH for the mainstream smoke of 20 cigarettes as determined using techniques described by Harris et al, supra.

The data in Table V indicate that the various cigarettes of this invention having high nicotine content cut filler (i.e., more than 2.5 percent total blend nicotine) exhibit FTC "tar" and nicotine deliveries comparable to the control cigarette. The various cigarettes also exhibit comparable FTC "tar" to nicotine ratios and puff counts. However, cigarettes of the invention (i.e., Sample Nos. 14-16 which contain levulinic acid additive) exhibit reduced average smoke pH when compared to a control (i.e., Sample No. C-6 which does not have the levulinic acid additive).

Organoleptic evaluation of the samples indicates that the cigarettes of the invention are smooth smoking while the control sample is very harsh. The mildness of Sample Nos. 15 and 16 is considered comparable. The cigarettes of the invention yield good tobacco taste, strength and smoking satisfaction. The control sample is very strong, and the overpowering sensation provided thereby is not satisfying.

Claims

1. A cigarette having smokable material contained in a circumscribing outer wrapping material, the cigarette having (i) a ratio of FTC "tar" to FTC nicotine of less than 9, (ii) a nicotine content greater than 2,25 %, based on the dry weight of the smokable material, and (iii) levulinic acid in dissociated and/or nondissociated form incorporated therein in an amount greater than 1 %, based on the dry weight of the smokable material.
2. The cigarette of Claim 1 wherein the nicotine content thereof is greater than 2.5 percent, based on the dry weight of the smokable material.
3. The cigarette of Claim 1 wherein the nicotine content thereof is greater than 3 percent, based on the dry weight of the smokable material.
4. The cigarette of Claim 1, 2 or 3 wherein the levulinic acid is incorporated therein in an amount greater than 2 percent, based on the dry weight of the smokable material.
5. The cigarette of Claim 1, 2 or 3 wherein the levulinic acid is incorporated therein in an amount greater than 3 percent, based on the dry weight of the smokable material.
6. The cigarette of one or several of the preceding claims wherein essentially all of the levulinic acid is in nondissociated form.
7. The cigarette of one or several of claims 1 to 5 wherein at least a portion of the levulinic acid is provided in the form of nicotine levulinate.
8. The cigarette of one or several of claims 1 to 7 having a ratio of FTC "tar" to FTC nicotine of less than 7.
9. The cigarette of Claim 8 having a ratio of FTC "tar" to FTC nicotine within the range of 3 to 6.
10. The cigarette of one or several of the preceding claims wherein the smokable material is a blend of tobacco materials.
11. The cigarette of one or several of the preceding claims and including a filter element, at least a portion of the levulinic acid being present within the filter element.

Patentansprüche

1. Zigarette mit rauchbarem Material, welches von einem begrenzenden äußeren Umhüllungsmaterial aufgenommen wird, wobei die Zigarette
 - (i) ein Verhältnis von FTC "Teer" zu FTC Nikotin von weniger als 9;
 - (ii) einen Nikotingehalt von mehr als 2,25 %, bezogen auf das Trockengewicht des rauchbaren Materials, und
 - (iii) im rauchbaren Material mehr als 1 %, bezogen auf dessen Trockengewicht, Lävulinsäure in dissoziierter und/oder nicht-dissoziierter Form hat.
2. Zigarette nach Anspruch 1, deren Nikotingehalt, bezogen auf das Trockengewicht des rauchbaren Materials, größer als 2,5 % ist.
3. Zigarette nach Anspruch 1, deren Nikotingehalt, bezogen auf das Trockengewicht des rauchbaren Materials, größer als 3 % ist.
4. Zigarette nach Anspruch 1, 2 oder 3, deren Lävulinsäuregehalt, bezogen auf das Trockengewicht des rauchbaren Materials, größer als 2 % ist.

5. Zigarette nach Anspruch 1, 2 oder 3, deren Lävulinsäuregehalt, bezogen auf das Trockengewicht des rauchbaren Materials, größer als 3 % ist.
6. Zigarette nach einem oder mehreren der vorstehenden Ansprüche, in der im wesentlichen die gesamte Lävulinsäure in nicht-dissoziierter Form vorliegt.
7. Zigarette nach einem oder mehreren der Ansprüche 1 bis 5, in der mindestens ein Teil der Lävulinsäure in Form von Nikotinlävulinat vorliegt.
8. Zigarette nach einem oder mehreren der Ansprüche 1 bis 7, welche ein Verhältnis von FTC "Teer" zu FTC Nikotin von weniger als 7 hat.
9. Zigarette nach Anspruch 1, welche ein Verhältnis von FTC "Teer" zu FTC Nikotin von 3 bis 6 hat.
10. Zigarette nach einem oder mehreren der vorstehenden Ansprüche, bei der das rauchbare Material eine Mischung aus Tabakmaterialien ist.
11. Zigarette nach einem oder mehreren der vorstehenden Ansprüche, welche ein Filterelement besitzt, in dem sich wenigstens ein Teil der Lävulinsäure befindet.

Revendications

1. Cigarette ayant un produit fumable contenu dans une couverture extérieure l'enveloppant, la cigarette ayant (i) un rapport du "goudron" FTC à la nicotine FTC inférieur à 9, (ii) une teneur en nicotine supérieure à 2,25%, sur base du poids sec du produit fumable, et (iii) de l'acide lévulinique sous sa forme dissociée et/ou non dissociée incorporé en une quantité supérieure à 1%, sur base du poids sec du produit fumable.
2. Cigarette selon la revendication 1, où la teneur en nicotine est supérieure à 2,5%, sur base du poids sec du produit fumable.
3. Cigarette selon la revendication 1, où la teneur en nicotine est supérieure à 3%, sur base du poids sec du produit fumable.
4. Cigarette selon la revendication 1, 2 ou 3, où l'acide lévulinique est incorporé en une quantité supérieure à 2%, sur base du poids sec du produit fumable.
5. Cigarette selon la revendication 1, 2 ou 3, où l'acide lévulinique est incorporé en une quantité supérieure à 3%, sur base du poids sec du produit fumable.
6. Cigarette selon une ou plusieurs des revendications précédentes, où tout l'acide lévulinique est essentiellement sous la forme non dissociée.
7. Cigarette selon une ou plusieurs des revendications 1 à 5, où au moins une partie de l'acide lévulinique est apporté sous la forme de lévulinate de nicotine.
8. Cigarette selon une ou plusieurs des revendications 1 à 7, ayant un rapport du "goudron" FTC à la nicotine FTC inférieur à 7.
9. Cigarette selon la revendication 8, ayant un rapport du "goudron" FTC à la nicotine FTC dans l'intervalle de 3 à 6.
10. Cigarette selon une ou plusieurs des revendications précédentes, où le produit fumable est un mélange de produits tabagiques.
11. Cigarette selon une ou plusieurs des revendications précédentes et incluant un bout filtrant, une partie au moins de l'acide lévulinique étant présente dans le bout filtrant.

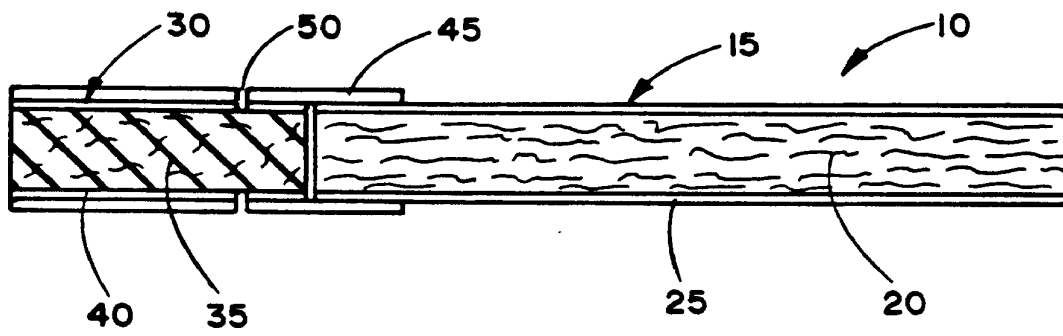


FIG. 1

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
12 July 2007 (12.07.2007)

PCT

(10) International Publication Number
WO 2007/078273 A1

(51) International Patent Classification:
A24F 1/24 (2006.01)

(21) International Application Number:
PCT/US2005/046546

(22) International Filing Date:
22 December 2005 (22.12.2005)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant (for all designated States except US): **AUGITE INCORPORATION** [US/US]; 80 Wall Street, Suite 818, New York, NY 10005 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **LIU, Zhen** [CN/CN]; 3 Garden Road, Central Hongkong (CN).

(74) Agents: **COSTELLIA, Jeffrey, L.** et al.; Nixon Peabody LLP, 401 9th Street, N.w., Suite 900, Washington, DC 20004 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

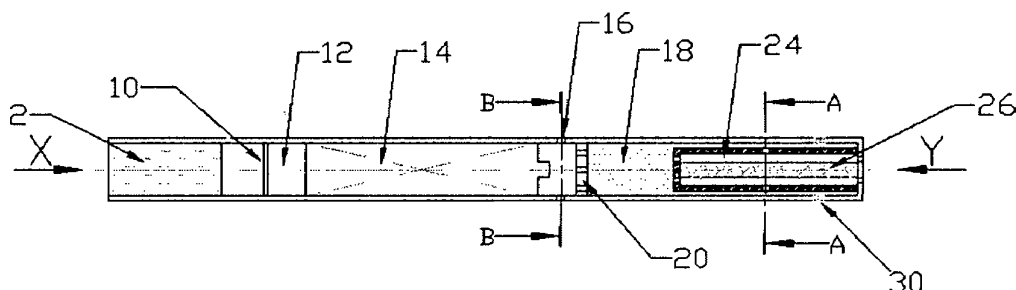
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: NO-TAR ELECTRONIC SMOKING UTENSILS



(57) Abstract: No-tar electronic smoking utensils includes a container (18) formed of a porous material for storing a liquid mixture. The container communicates with a heater vapouriser (24) via a series of small apertures (28). The heater is in the form of a spirally wound electrical heater (26) mounted on an electrical insulating support. Battery supply means are provided for the heater. The heater vapouriser communicates with a mouthpiece. In use, suction on the mouthpiece by the user causes air to be drawn through the porous container for liquid, over the heated vapouriser, into the mouthpiece and into the mouth of the user.

WO 2007/078273 A1

NO-TAR ELECTRONIC SMOKING UTENSILS

TECHNICAL FIELD

5

The present invention relates to no-tar electronic smoking utensils such as, for example, cigarettes, cigars and cigarette holders.

BACKGROUND

10

Cigarettes are well known in which one end of a tobacco filled cigarette is held in the mouth of the user and the other end of the cigarette is ignited by a match or a lighter and the user draws on one end of the cigarette to draw the tobacco smoke through the cigarette into the mouth/lungs of the user. The health dangers of tobacco smoking are well documented and many products have appeared on the market in an attempt to assist smokers to cease smoking tobacco products or to provide a more healthy tobacco substitute.

20

One such product is a "flameless electronic atomising cigarette" described in Malaysian patent application 03111582.9. The product is a non-combustible simulated cigarette and the user draws on one end of the "cigarette" to draw a nicotine vapour through the cigarette via a solution having a controlled amount of nicotine. The lack of a flame avoids inhaling tar and other unhealthy tobacco products, and the user can also control the amount of nicotine inhaled. The nicotine mixture of the prior art electronic cigarette is pumped through the device and is atomised by the use of a high frequency generator, a piezoelectric ultrasonic atomiser and a high-temperature gasification jet tube. The resulting vapour, lacking the

25

30

conventional tar and unhealthy by- products, but including a controlled amount of nicotine, is inhaled by the user.

SUMMARY OF INVENTION

5

It is an object of the present invention to provide a no-tar electronic smoking utensils which is a suitable alternative to known products and/or is of a simpler construction in comparison to known products.

10

In accordance with one aspect of the invention, there is provided a no-tar electronic smoking utensils including:

a container for a liquid,

a vapouriser including heater means adapted to vapourise the

15

liquid,

wherein air can be drawn by the suction of the user over the container and vapouriser to form a simulated smoke vapour.

20

Preferably, in contrast to the above prior art device the vapourisation is effected solely or principally by the air distribution through the container in combination with the heat from the heating means.

25

Preferably, in contrast to the above prior art device the flow of fluids through the cigarette is caused solely or principally by the suction of the user.

30

Thus, the simulated cigarette of the present invention is of a simpler construction, easier to manufacture and more cost effective than the above prior art device.

Preferably, at least a portion of the container is formed of a porous material to facilitate distribution of the liquid through the container, prior to being fed to the heater means. Suitable materials include, for example, foamed metal, foamed ceramic or special fibre.

5

In a preferred arrangement the heater means includes an electrical heater mounted on an electrical insulating support, for example a spirally wound heater wire.

10 The liquid mixture may be formed from any suitable materials/chemicals. The mixture could include a controlled amount of nicotine, however the mixture need not include a nicotine content.

15 Indicating/monitoring means may be included for the purpose of indicating a range of activities such as when a pre-set level of nicotine has been reached, when the unit is switched on or when the liquid in the container is low.

20 In a preferred arrangement simulated tobacco is provided in the tip end of the smoking article to give the article the appearance of a conventional smoking article.

The no-tar electronic smoking utensils preferably includes electrical
25 supply means, such as a battery, to supply power to the heater and/or the indicator means. In a preferred arrangement power supply switch means are located adjacent the mouthpiece end of the cigarette, the power supply switch means being adapted to be activated by the lips of the user.

30

In accordance with another aspect of the invention, there is provided a simulated cigarette including a container formed of a

porous material for storing a liquid mixture, the container communicating with a heater vapouriser via a series of apertures, said vapouriser including a spirally wound electrical heater mounted on an electrical insulating support, battery supply means for the heater, said heater vapouriser communicating with a mouthpiece, whereby in use, suction on the mouthpiece by the user causes air to be drawn through the porous container for liquid, over the heated vapouriser, into the mouthpiece and into the mouth of the user.

10 **SPECIFIC EXAMPLE OF THE INVENTION**

In order to better understand the invention, an example will now be described with reference to the following drawings, in which:

15 FIG 1 is an enlarged side view of a simulated cigarette constructed in accordance with the invention,

FIG 2 is a cross- sectional side view of the simulated cigarette of FIG 1,

20

FIG 3 is a tip end view of the simulated cigarette of FIG 1 looking in the direction of arrow X,

FIG 4 is a mouthpiece end view of the simulated cigarette of FIG 1 looking in the direction of arrow Y,

25

FIG 5 is a cross-sectional end view taken along the lines AA of FIG 2,

30 FIG 6 is a cross-sectional end view taken along the lines BB of FIG 2, and

FIG 7 is a schematic diagram of the electrical components of the example shown in FIG 1.

Referring to FIG 1 of the example, the simulated cigarette is of the
5 general size and shape of a conventional elongated cylindrical cigarette, having a tip end 2 and a mouthpiece end 4.

In broad terms, the simulated cigarette of the example is provided with a container for a liquid mixture, a heater for vapourising the
10 liquid, apertures for passage of air/mixture vapour through the cigarette into the mouth of the user, and a battery for supplying power to the heater.

Referring to FIGS 1 and 2, the simulated cigarette is provided with
15 an outer casing 6. The tip end 2 of the casing 6 is provided with simulated tobacco to give the simulated cigarette the appearance of a conventional cigarette. Modifications, such as choice and feel of materials, obvious to those skilled in the art, could also be made to give the simulated cigarette the look and feel of a conventional
20 cigarette.

Adjacent and inner the tip end 2 of the cigarette and mounted on the cigarette casing 6 is a light emitting diode (LED) 8. The LED is for the purpose of monitoring/indicating, amongst other things, the
25 level of liquid in the container and when a pre-set level of nicotine has been reached.

Located inner and adjacent of the simulated tobacco is a printed circuit board (PCB) control unit 10 for controlling the electrics of the cigarette.
30

Adjacent and inner of the PCB 10, is a cylindrical battery chamber 12 for housing a battery 14. The cigarette outer casing 6, adjacent

the battery chamber 12 is provided with a plurality of apertures 16 to permit entry of air into the battery chamber. Adjacent and inner of the battery chamber 12 is a cylindrical liquid container 18 separated from the battery chamber by a dividing wall 20. The
5 dividing wall 20 is provided with a plurality of apertures 22 to permit entry of air from the battery chamber into the liquid container.

The container liquid mixture can be fed into the container 18 via a
10 one-way valve (not shown) mounted through the wall of the cigarette casing 6. The liquid container 18 is formed of porous inorganic material. The porous material of the liquid container facilitates the distribution and the mixing of the air and liquid mixture.

15 A cylindrical vapouriser heater assembly housing 24 is mounted within a central bore provided in the mouthpiece end of the liquid container 18. The vapouriser heater assembly housing houses a heater wire 26 spirally wound on a central ceramic insulating rod.
20 The walls of the heater housing 24 are provided with a plurality of apertures 28 to permit entry of the liquid/air from the liquid container 18 into the heater housing 24.

Adjacent the mouthpiece end 4 of the cigarette and mounted on
25 the cigarette outer casing 6 is a switch 30 activated, in use, by the mouth of the user for the purpose of switching on the battery power supply.

As indicated above, the liquid of the container may contain any
30 suitable chemicals, and may be provided with or without nicotine.

The approximate percentages of ingredients for a mixture containing nicotine are as follows:

1,2 propylene glycol 81%, nicotine 7%, distilled water 6%, glycerol triacetin 5%, formic acid, acetic acid, acetol and fragrance etc. 1%.

5

The approximate percentages of ingredients for a mixture without nicotine are as follows:

1,2 propylene glycol 88%, distilled water 6%, glycerol triacetin 5%, formic acid, acetic acid, acetol and fragrance etc. 1%.

10

In operation, the switch 30 is activated by the lips of the user touching the switch 30 thus switching on the battery power supply. As best seen in the electrical schematic diagram of FIG 7, battery power is supplied to the PCB control unit 10, the LED 8 and the vapouriser heater 26.

15

As the user draws on the cigarette mouthpiece, air is drawn into the battery chamber, into the liquid container to mix with the liquid mixture, and into the heater assembly. The resulting vapour is drawn into the mouth of the user.

20

25

30

CLAIMS:

1. A no-tar electronic smoking utensils including:
a container for a liquid,
5 a vapouriser including heater means adapted to vapourise the liquid,
wherein air can be drawn by the suction of the user over the container and vapouriser to form a simulated smoke vapour.
- 10 2. A no-tar electronic smoking utensils according to Claim 1 wherein the vapourisation is effected solely or principally by the air distribution through the container in combination with the heat from the heating means.
- 15 3. A no-tar electronic smoking utensils according to Claim 1 or Claim 2 wherein the flow of fluids through the cigarette is caused solely or principally by the suction of the user.
- 20 4. A no-tar electronic smoking utensils according to any preceding claim wherein at least a portion of the container is formed of a porous material to facilitate distribution of the liquid through the container, prior to being fed to the heater means.
- 25 5. A no-tar electronic smoking utensils according to any preceding claim wherein the heater means includes an electrical heater mounted on an electrical insulating support.
6. A no-tar electronic smoking utensils according to any preceding claim wherein the liquid includes a controlled amount of nicotine.

30

7. A no-tar electronic smoking utensils according to any preceding claim including indicator means for the purpose of indicating when a pre-set level of nicotine has been reached.

5 8. A no-tar electronic smoking utensils according to any preceding claim including simulated tobacco at a first or tip end of the smoking article to give the article the appearance of a conventional smoking article.

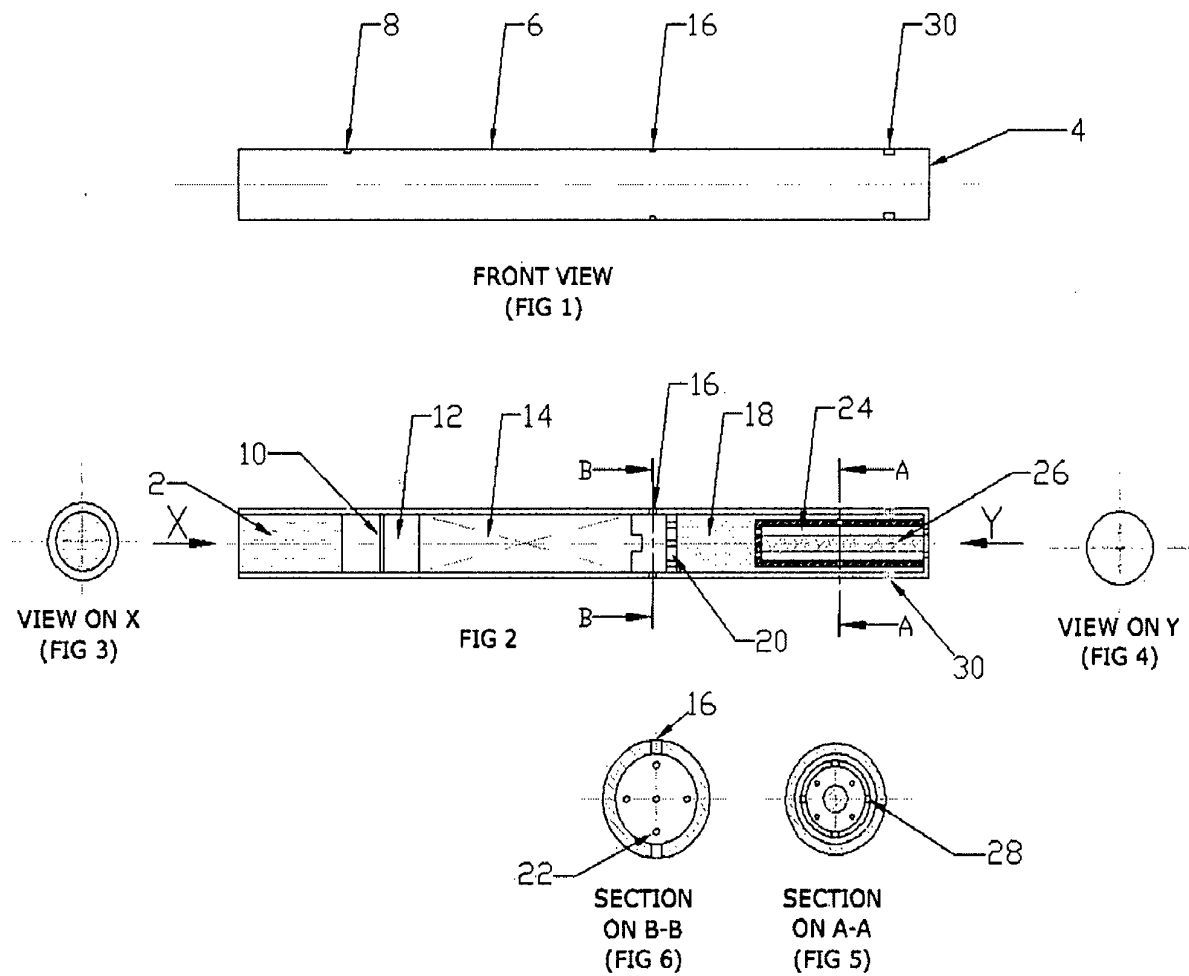
10 9. A simulated cigarette according to any preceding claim including electrical supply means to supply power to the heater and/or the indicator means, power supply switch means located adjacent the second or mouthpiece end of the cigarette, said power supply switch means being adapted to be activated by the lips of the user.

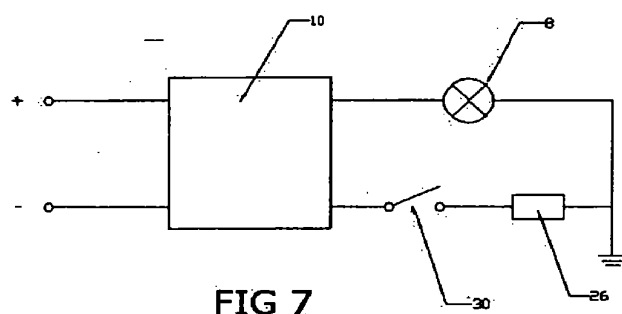
15

10. A simulated cigarette including a container formed of a porous material for storing a liquid mixture, the container communicating with a heater vapouriser via a series of apertures, said vapouriser including a spirally wound electrical heater mounted on an electrical
20 insulating support, battery supply means for the heater, said heater vapouriser communicating with a mouthpiece, whereby in use, suction on the mouthpiece by the user causes air to be drawn through the porous container for liquid, over the heated vapouriser, into the mouthpiece and into the mouth of the user.

25

30





INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/46546

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A 24 F 01/24

USPC: 131/194,329,347

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 131/194,329,347

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,947,874 A (BROOKS et al) 14 August 1990 (14.08.1990), see entire document.	1-5
--		-----
Y		6-10

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 May 2006 (22.05.2006)

Date of mailing of the international search report

27 JUN 2006

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Authorized officer

Dionne Walls Mayes

Telephone No. (571) 272-1700



- (51) International Patent Classification:
A24B 15/16 (2006.01) A24F 47/00 (2006.01)
- (21) International Application Number:
PCT/US2014/046903
- (22) International Filing Date:
16 July 2014 (16.07.2014)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/856,286 19 July 2013 (19.07.2013) US
- (71) Applicant: **ALTRIA CLIENT SERVICES INC.**
[US/US]; 6601 West Broad Street, Richmond, Virginia
23230 (US).
- (72) Inventors: **LIPOWICZ, Peter**; 6003 Sedgefield Terrace,
Midlothian, Virginia 23112 (US). **MARCQ, Pauline**; 33
W Lock Lane #1, Richmond, Virginia 23226 (US).
KOBAL, Gerd; 3124 Rock Cress Lane, Sandy Hook, Vir-
ginia 23153 (US). **MISHRA, Munmaya K.**; 1631 Sabot
Creek Drive, Manakin Sabot, Virginia 23103 (US).
KARLES, Georgios D.; 4025 Huntstead Way, Richmond,
Virginia 23233 (US). **LI, San**; 1313 Goswick Ridge Road,
Midlothian, Virginia 23114 (US).
- (74) Agents: **SKIFF, Peter K.** et al.; Buchanan Ingersoll &
Rooney PC, P. O. Box 1404, Alexandria, Virginia 22313-
1404 (US).
- (81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

- (84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii))

Published:

- without international search report and to be republished
upon receipt of that report (Rule 48.2(g))

(54) Title: LIQUID AEROSOL FORMULATION OF AN ELECTRONIC SMOKING ARTICLE

(57) Abstract: A liquid aerosol formulation for an electronic smoking article includes an aerosol former, water, nicotine, and an acid including tartaric acid. The acid is included in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8.



WO 2015/009862 A2

LIQUID AEROSOL FORMULATION OF AN ELECTRONIC SMOKING ARTICLE

Cross-Reference to Related Application

[0001] This application claims priority under 35 U.S.C. §119(e) to U.S. provisional Application No. 61/856,286, filed on July 19, 2013, the entire content of which is incorporated herein by reference thereto.

Background

[0002] A lit-end smoking article produces an aerosol known to create pleasant sensory experience for adult smokers, including a low to moderate harshness response in the throat and a perceived warmth in the chest. The preferred levels of harshness in the throat and perceived warmth in the chest will differ amongst adult cigarette smokers.

Object of the Preferred Embodiments

[0003] An object of the teachings herein is the achievement of an electronic smoking article, such as an electronic cigarette, which is capable of providing a pleasant sensory experience for adult smokers that is similar to those enjoyed by them while smoking a lit end cigarette.

[0004] Another object of the teachings herein is the achievement of an electronic smoking article which is capable of providing a sensory experience comprising levels of harshness in the throat and perceived warmth in the chest that are similar to those experienced by adult smokers when smoking a lit end cigarette.

Summary of Selected Features

[0005] In an embodiment, a liquid aerosol formulation operative in an electronic smoking article having a heater operating temperature is provided. The liquid aerosol formulation comprises an aerosol former, water in an amount of 0% to about 40% by weight based on the weight of the liquid aerosol formulation, nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation, and an acid having a melting point and/or a boiling point of at least about 150°C and such that the acid volatilizes at the heater temperature and is condensable at ambient temperatures. The acid is included in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8. The liquid aerosol formulation forms an aerosol having a particulate phase and

a gas phase when heated during operation of the electronic smoking article. The particulate phase contains protonated nicotine and the gas phase contains unprotonated nicotine. The gas phase nicotine content of the aerosol is less than about 1% of a total nicotine content of the aerosol.

[0006] The liquid aerosol formulation can also comprise at least one flavorant in an amount ranging from about 0.2% to about 15% by weight. Moreover, the aerosol former is selected from the group consisting of propylene glycol, glycerin and combinations thereof. The aerosol former is included in an amount ranging from about 40% by weight to about 90% by weight. The acid preferably has a boiling point ranging from about 150°C to about 250°C or the acid preferably has a melting point ranging from about 150°C to about 250°C. In an embodiment, the acid has a melting point and/or a boiling point of about 150°C to about 300°C. In a preferred embodiment, the liquid formulation comprises glycerin and propylene glycol in a ratio of about 2:3 or greater. Moreover, nicotine is included in an amount ranging from about 2 % by weight to about 10% by weight. The particulate phase comprises particles ranging in size from about 0.2 micron to about 2 microns. The acid is included in an amount ranging from about 0.1% by weight to about 15% by weight. The water can be included in an amount of about 5% by weight to about 40% by weight based on the weight of the liquid aerosol formulation or in an amount of about 5% to about 15% by weight based on the weight of the liquid aerosol formulation. In an embodiment, the liquid aerosol formulation has a pH ranging from about 5.5 to about 8.

[0007] In an embodiment, the liquid aerosol formulation also comprises ammonia or an ammonia containing compound in an amount sufficient to reduce the pH of the liquid aerosol formulation by about 1 to about 2 pH units.

[0008] The acid is selected from the group consisting of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid combinations thereof. In a preferred embodiment, the acid comprises tartaric acid. In another preferred embodiment, at least some of the acid and at least some of the nicotine is from a nicotine-acid salt. Also preferably, the nicotine-acid salt comprises nicotine bitartrate.

[0009] In another embodiment, an electronic smoking article operable to produce an aerosol which substantially replicates a sensory experience of smoking a lit-end cigarette is provided. The electronic smoking article comprises a heater, and a liquid aerosol formulation. The heater is operable to volatilize the liquid aerosol formulation and form an aerosol. The liquid aerosol formulation comprises an aerosol former, water in an amount of

0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation, nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation, and an acid in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8. The liquid aerosol formulation is capable of forming the aerosol having a particulate phase and a gas phase when heated by the heater. The particulate phase contains protonated nicotine and the gas phase contains unprotonated nicotine. The aerosol has a majority amount of the protonated nicotine and a minority amount of the unprotonated nicotine. The sensory experience includes a perception of chest warmth and moderate throat harshness during a puff.

[0010] In an embodiment, the heater comprises a capillary tube in fluid communication with a reservoir containing the liquid aerosol formulation. The reservoir is pressurized and comprises a mechanically or electrically operated valve at an outlet of the reservoir. The reservoir is compressible such that the liquid material is manually pumped to the capillary.

[0011] In an embodiment, the heater is a coil heater in communication with a filamentary wick which draws liquid from a reservoir via capillary action. The electronic smoking article further comprises an outer tube extending in a longitudinal direction, an inner tube within the outer tube, and the reservoir comprising an outer annulus between the outer tube and the inner tube. The coil heater is located in the inner tube and the filamentary wick is in communication with the reservoir and surrounded by the coil heater such that the wick delivers the liquid aerosol formulation to the coil heater and the coil heater heats the liquid aerosol formulation to a temperature sufficient to vaporize the liquid aerosol formulation and form the aerosol.

[0012] In an embodiment, a method of replicating a sensory experience of smoking a lit-end cigarette comprises heating a liquid aerosol formulation to form an aerosol. The liquid aerosol formulation comprises an aerosol former, water in an amount of 0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation, nicotine in an amount of about 2% or more by weight based on the weight of the liquid aerosol formulation, and an acid in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8. The aerosol has a particulate phase and a gas phase. The particulate phase contains protonated nicotine and the gas phase contains unprotonated nicotine. The unprotonated nicotine is preferably less than about 1% of a total nicotine content of the aerosol. The sensory experience includes a perception of chest warmth and moderate throat harshness during a puff. Moreover, the acid has a melting point and/or a

boiling point of at least about 150°C such that the acid volatilizes at a heater temperature and is condensable at ambient temperatures.

[0013] In another embodiment, a method of forming an aerosol with an electronic smoking article comprises heating a liquid aerosol formulation to a temperature sufficient to form an aerosol. The liquid aerosol formulation comprises an aerosol former, water in an amount of 0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation, nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation, and an acid in an amount sufficient to provide the liquid aerosol formulation a pH ranging from about 4 to about 8. The acid is operative upon the aerosol so as to reduce an amount of perceived throat harshness by a smoker in comparison to the aerosol being formed upon operation of the electronic smoking article without the acid.

[0014] In an embodiment, the acid comprises tartaric acid in an amount ranging from about 0.1% by weight to about 15% by weight based on the weight of the liquid aerosol formulation. Moreover, the liquid aerosol formulation can further comprise ammonia or an ammonia containing compound in an amount sufficient to reduce the pH of the final liquid aerosol formulation by about 1 to about 2 pH units.

[0015] In yet another embodiment, a method of forming a component of an electronic smoking article comprises preparing a liquid aerosol formulation by combining an aerosol former in an amount of at least about 50% by weight based on the weight of the liquid aerosol formulation and water in an amount of about 5% by weight to about 40% by weight based on the weight of the liquid aerosol formulation, adding nicotine bitartrate in an amount sufficient to establish a nicotine content of at least about 2% by weight to the liquid aerosol formulation, and filling a reservoir of a component of an electronic smoking article with the liquid aerosol formulation.

[0016] In another embodiment, an aerosol is produced by heating a liquid aerosol formulation in an electronic smoking article. The liquid aerosol formulation comprises nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation and an acid. The nicotine content is sufficient to produce a perception of chest warmth associated with smoking a lit end cigarette. The aerosol has a gas phase nicotine content of the aerosol of less than 1% of a total nicotine content of the aerosol. The acid is operative upon the aerosol so as to reduce an amount of perceived throat harshness by a smoker in comparison to the aerosol being formed upon operation of the electronic smoking article without the acid.

Brief Description of the Drawings

[0017] Figure 1 is a side view of an electronic smoking article constructed according to an embodiment.

[0018] Figure 2 is a cross-sectional view of an electronic smoking article according to an embodiment.

[0019] Figure 3 is a cross-sectional view of another embodiment of an electronic smoking article according to an embodiment.

[0020] Figure 4 is a cross-sectional view of an electronic smoking article according to an embodiment.

[0021] Figure 5 is a graphical representation showing the gas phase nicotine content per puff of an electronic smoking article including a liquid aerosol formulation not including at least one acid as compared to the gas phase nicotine content per puff of an electronic smoking article including a liquid aerosol formulation including at least one acid as described herein.

Detailed Description

[0022] In an embodiment, an electronic smoking article comprises a liquid supply (reservoir) containing a liquid aerosol formulation. The liquid aerosol formulation is delivered to a heater where the liquid aerosol formulation is heated and volatilized. As used herein, the term “electronic smoking article” is inclusive of all types of electronic smoking articles, regardless of form, size or shape, including electronic cigarettes, electronic cigars, electronic pipes, electronic hookahs and the like. Moreover, the liquid aerosol formulation can include tobacco flavors or instead, or in combination, include other suitable flavors.

[0023] In a preferred embodiment, the liquid aerosol formulation includes (comprises) an acid (as used herein “an acid” means one or more acids), which protonates nearly all of the molecular nicotine in the liquid formulation, so that upon heating of the liquid aerosol formulation in the electronic smoking article, an aerosol having a majority amount of protonated nicotine and a minority amount of unprotonated nicotine is produced, whereby only a minor portion of all the volatilized (vaporized) nicotine remains in the gas phase of the aerosol.

[0024] Preferably, the aerosol produced from the liquid aerosol formulation includes unprotonated nicotine in an amount ranging from about 0.1% to about 1.0% by weight based on the total nicotine content in the aerosol, more preferably about 0.1% to 0.5% by weight based on the total nicotine content in the aerosol. Since the majority of the nicotine in the aerosol is protonated, the aerosol contributes a sensory response of low to mild harshness in

the throat, even at elevated nicotine levels in the liquid aerosol formulation. Much of the foregoing occurs, because protonated nicotine is charged and does not enter or remain in a gas phase of the aerosol, but is instead found in a particulate phase of the aerosol.

[0025] Preferably, the acid: (a) is sufficiently, thermally stable to withstand a heating cycle of an electronic smoking article so that at least a substantial portion of the acid enters the gas vapor phase as an acid; (b) volatilizes at the heater temperature; and (c) is condensable at ambient temperatures. In a preferred embodiment, the acid has a melting point and/or a boiling point of at least about 150°C and is included in the liquid aerosol formulation in an amount sufficient to adjust the pH of the liquid aerosol formulation to about 4 to about 8, more preferably about 5.5 to about 8.

[0026] The liquid aerosol formulation disclosed herein forms an aerosol when vaporized in an electronic smoking article as shown in Figure 1. The electronic smoking article 60 comprises a replaceable cartridge (or first section) 70 and a reusable fixture (or second section) 72, which are coupled together at a threaded joint 74 or by other convenience such as a snug-fit, snap-fit, detent, clamp and/or clasp.

[0027] As shown in Figure 3, the first section 70 can house a mouth end insert 20, a capillary aerosol generator including a capillary (capillary tube) 18, a heater 19 to heat at least a portion of the capillary 18, a reservoir 14 and optionally a valve 40. Alternatively, as shown in Figure 4, the first section 70 can house a mouth end insert 20, a heater 319, a flexible, filamentary wick 328 and a reservoir 314 as discussed in further detail below.

[0028] The second section 72 can house a power supply 12 (shown in Figures 2, 3 and 4), control circuitry 11, and optionally a puff sensor 16 (shown in Figures 3 and 4). The threaded portion 74 of the second section 72 can be connected to a battery charger when not connected to the first section 70 for use so as to charge the battery.

[0029] As shown in Figure 2, the electronic smoking article 60 can also include a middle section (third section) 73, which can house the reservoir 14, the heater 19, and the valve 40. The middle section 73 can be adapted to be fitted with a threaded joint 74' at an upstream end of the first section 70 and a threaded joint 74 at a downstream end of the second section 72. In this embodiment, the first section 70 houses the mouth end insert 20, while the second section 72 houses the power supply 12 and control circuitry.

[0030] Preferably, the first section 70, the second section 72 and the optional third section 73 include an outer cylindrical housing 22 extending in a longitudinal direction along the length of the electronic smoking article 60. Moreover, in one embodiment, the middle section 73 is disposable and the first section 70 and/or second section 72 are reusable. In

another embodiment, the first section 70 can also be replaceable so as to avoid the need for cleaning the capillary 18 and/or heater 19. The sections 70, 72, 73 can be attached by threaded connections whereby the middle section 73 can be replaced when the liquid aerosol formulation in the reservoir 14 is used up.

[0031] It is contemplated that the first section 70 and the second section 72 may be unitary and without threaded connections.

[0032] As shown in Figure 2, the outer cylindrical housing 22 can include a cutout or depression 102 which allows a smoker to manually apply pressure to the reservoir 14. Preferably, the outer cylindrical housing 22 is flexible and/or compressible along the length thereof and fully or partially covers the reservoir 14. The cutout or depression 102 can extend partially about the circumference of the outer cylindrical housing 22. Moreover, the reservoir 14 is compressible such that when pressure is applied to the reservoir, liquid is pumped from the reservoir 14 to the capillary 18. A pressure activated switch 44 can be positioned beneath the reservoir 14. When pressure is applied to the reservoir 14 to pump liquid, the switch is also pressed and a heater 19 is activated. The heater 19 can be a portion of the capillary 18. By applying manual pressure to the pressure switch, the power supply 12 is activated and an electric current heats the liquid in the capillary 18 via electrical contacts so as to volatilize the liquid.

[0033] In the embodiment of Figure 2, the reservoir 14 is a tubular, elongate body formed of an elastomeric material so as to be flexible and/or compressible when squeezed. Preferably, the elastomeric material can be selected from the group consisting of silicone, plastic, rubber, latex, and combinations thereof.

[0034] Preferably, the compressible reservoir 14 has an outlet 17 which is in fluid communication with a capillary 18 so that when squeezed, the reservoir 14 can deliver a volume of liquid material to the capillary 18. Simultaneous to delivering liquid to the capillary, the power supply 12 is activated upon application of manual pressure to the pressure switch and the capillary 18 is heated to form a heated section wherein the liquid material is volatilized. Upon discharge from the heated capillary 18, the volatilized material expands, mixes with air and forms an aerosol.

[0035] Preferably, the reservoir 14 extends longitudinally within the outer cylindrical housing 22 of the first section 70 (shown in Figures 3 and 4) or the middle section 73 (shown in Figure 2). Moreover, the reservoir 14 comprises a liquid aerosol formulation which is volatilized when heated and forms an aerosol when discharged from the capillary 18.

[0036] In the embodiments shown in Figures 2 and 3, the capillary 18 includes an inlet end 62 in fluid communication with the outlet 17 of the reservoir 14, and an outlet end 63 operable to expel volatilized liquid material from the capillary 18. In a preferred embodiment, as shown in Figures 2 and 3, the reservoir 14 may include the valve 40.

[0037] As shown in Figure 2, the valve 40 can be a check valve that is operable to maintain the liquid material within the reservoir, but opens when the reservoir 14 is squeezed and pressure is applied. Preferably, the check valve 40 opens when a critical, minimum pressure is reached so as to avoid inadvertent dispensing of liquid material from the reservoir 14 or activating the heater 19. Preferably, the critical pressure needed to open the check valve 40 is essentially equal to or slightly less than the pressure required to press a pressure switch 44 to activate the heater 19. Preferably, the pressure required to press the pressure switch 44 is high enough such that accidental heating is avoided. Such arrangement avoids activation of the heater 19 in the absence of liquid being pumped through the capillary.

[0038] Advantageously, the use of a check valve 40 aids in limiting the amount of liquid that is drawn back from the capillary upon release of pressure upon the reservoir 14 (and/or the switch 44) if manually pumped so as to avoid air uptake into the reservoir 14. Presence of air degrades pumping performance of the reservoir 14.

[0039] Once pressure upon the reservoir 14 is relieved, the valve 40 closes. The heated capillary 18 discharges liquid remaining downstream of the valve 40.

[0040] Optionally, a critical flow orifice 41 is located downstream of the check valve 40 to establish a maximum flow rate of liquid to the capillary 18.

[0041] As shown in Figure 3, in other embodiments, the valve 40 can be a two-way valve and the reservoir 14 can be pressurized. For example, the reservoir 14 can be pressurized using a pressurization arrangement 405 which applies constant pressure to the reservoir 14. For example, pressure can be applied to the reservoir 14 using an internal or external spring and plate arrangement which constantly applies pressure to the reservoir 14. Alternatively, the reservoir 14 can be compressible and positioned between two plates that are connected by springs or the reservoir 14 could be compressible and positioned between the outer housing and a plate that are connected by a spring so that the plate applies pressure to the reservoir 14.

[0042] Preferably, the capillary 18 of Figures 2 and 3 has an internal diameter of 0.01 to 10 mm, preferably 0.05 to 1 mm, and more preferably 0.05 to 0.4 mm. Capillaries of smaller diameter provide more efficient heat transfer to the fluid because, with the shorter distance to the center of the fluid, less energy and time is required to vaporize the liquid.

[0043] Also preferably, the capillary 18 may have a length of about 5 mm to about 72 mm, more preferably about 10 mm to about 60 mm or about 20 mm to about 50 mm. In one embodiment, the capillary 18 is substantially straight. In other embodiments, the capillary 18 is coiled and/or includes one or more bends therein to conserve space and/or accommodate a long capillary.

[0044] In these embodiments, the capillary 18 is formed of a conductive material, and thus acts as its own heater 19 by passing current through the capillary. The capillary 18 may be any electrically conductive material capable of being resistively heated, while retaining the necessary structural integrity at the operating temperatures experienced by the capillary 18, and which is non-reactive with the liquid material. Suitable materials for forming the capillary 18 are selected from the group consisting of stainless steel, copper, copper alloys, porous ceramic materials coated with film resistive material, Inconel[®] available from Special Metals Corporation, which is a nickel-chromium alloy, nichrome, which is also a nickel-chromium alloy, and combinations thereof.

[0045] In one embodiment, the capillary 18 is a stainless steel capillary 18, which serves as a heater 19 via electrical leads 26 attached thereto for passage of direct or alternating current along a length of the capillary 18. Thus, the stainless steel capillary 18 is heated by resistance heating. The stainless steel capillary 18 is preferably circular in cross section and may be formed of tubing suitable for use as a hypodermic needle of various gauges. For example, the capillary 18 may comprise a 32 gauge needle has an internal diameter of 0.11 mm and a 26 gauge needle has an internal diameter of 0.26 mm.

[0046] In another embodiment, the capillary 18 may be a non-metallic tube such as, for example, a glass tube. In such an embodiment, the heater 19 is formed of a conductive material capable of being resistively heated, such as, for example, stainless steel, nichrome or platinum wire, arranged along the glass tube. When the heater arranged along the glass tube is heated, liquid material in the capillary 18 is heated to a temperature sufficient to at least partially volatilize liquid material in the capillary 18.

[0047] Preferably, at least two electrical leads 26 are bonded to a metallic capillary 18. In the preferred embodiment, the at least two electrical leads 26 are brazed to the capillary 18. Preferably, one electrical lead 26 is brazed to a first, upstream portion 101 of the capillary 18 and a second electrical lead 26 is brazed to a downstream, end portion 107 of the capillary 18, as shown in Figures 2 and 3.

[0048] In use, once the capillary 18 of Figures 2 and 3 is heated, the liquid material contained within a heated portion of the capillary 18 is volatilized and ejected out of the outlet 63 where it expands and mixes with air and forms an aerosol in a mixing chamber 240.

[0049] As noted above, the liquid aerosol formulation can also be used in an electronic smoking article including a heater 319 and a filamentary wick 328 as shown in Figure 4. The first section 70 includes an outer tube (or casing) 22 extending in a longitudinal direction and an inner tube (or chimney) 362 coaxially positioned within the outer tube 22. Preferably, a nose portion 361 of an upstream gasket (or seal) 320 is fitted into an upstream end portion 365 of the inner tube 362, while at the same time, an outer perimeter 367 of the gasket 320 provides a liquid-tight seal with an interior surface 397 of the outer casing 22. The upstream gasket 320 also includes a central, longitudinal air passage 315, which opens into an interior of the inner tube 362 that defines a central channel 321. A transverse channel 333 at an upstream portion of the gasket 320 intersects and communicates with the central, longitudinal air passage 315 of the gasket 320. This channel 333 assures communication between the central, longitudinal air passage 315 and a space 335 defined between the gasket 320 and a threaded connection 74.

[0050] Preferably, a nose portion 393 of a downstream gasket 310 is fitted into a downstream end portion 381 of the inner tube 362. An outer perimeter 382 of the gasket 310 provides a substantially liquid-tight seal with the interior surface 397 of the outer casing 22. The downstream gasket 310 includes a central channel 384 disposed between the central passage 321 of the inner tube 362 and the mouth end insert 20.

[0051] In this embodiment, the reservoir 314 is contained in an annulus between the inner tube 362 and the outer casing 22 and between the upstream gasket 320 and the downstream gasket 310. Thus, the reservoir 314 at least partially surrounds the central air passage 321. The reservoir 314 comprises a liquid material and optionally a liquid storage medium (not shown) operable to store the liquid material therein.

[0052] The inner tube 362 has the central air passage 321 extending therethrough which houses the heater 319. The heater 319 is in contact with the filamentary wick 328, which preferably extends between opposing sections of the reservoir 314 so as to deliver the liquid aerosol formulation from the reservoir 314 to the heater 319.

[0053] Preferably, the electronic smoking article 60 of each embodiment described herein also includes at least one air inlet 440. As shown in Figure 4, the at least one air inlet 440 can be located upstream of the heater 319.

[0054] In the embodiments shown in Figures 2 and 3, the at least one air inlet 440 is

preferably arranged downstream of the capillary 18 so as to minimize drawing air along the capillary and thereby avoid cooling of the capillary 18 during heating cycles.

[0055] In the embodiments, the at least one air inlet 440 includes one or two air inlets. Alternatively, there may be three, four, five or more air inlets. Altering the size and number of air inlets 440 can also aid in establishing the resistance to draw of the electronic smoking article 60.

[0056] The power supply 12 of each embodiment can include a battery arranged in the electronic smoking article 60. The power supply 12 is operable to apply voltage across the heater 19 associated with the capillary 18, as shown in Figures 2 and 3, or the heater 319 associated with the filamentary wick 328, as shown in Figure 4. Thus, the heater 19, 319 volatilizes liquid material according to a power cycle of either a predetermined time period, such as a 2 to 10 second period.

[0057] Preferably, the electrical contacts or connection between the heater 19, 319 and the electrical leads 26 are highly conductive and temperature resistant while the heater 19, 319 is highly resistive so that heat generation occurs primarily along the heater 19 and not at the contacts.

[0058] The battery can be a Lithium-ion battery or one of its variants, for example a Lithium-ion polymer battery. Alternatively, the battery may be a Nickel-metal hydride battery, a Nickel cadmium battery, a Lithium-manganese battery, a Lithium-cobalt battery or a fuel cell. In that case, preferably, the electronic smoking article 60 is usable by a smoker until the energy in the power supply is depleted. Alternatively, the power supply 12 may be rechargeable and include circuitry allowing the battery to be chargeable by an external charging device. In that case, preferably the circuitry, when charged, provides power for a pre-determined number of puffs, after which the circuitry must be re-connected to an external charging device.

[0059] Preferably, the electronic smoking article 60 of each embodiment also includes control circuitry 11 (shown in Figures 2, 3 and 4), which can be on a printed circuit board. The control circuitry 11 can also include a heater activation light 27 that is operable to glow when the heater 19, 319 is activated. Preferably, the heater activation light 27 comprises at least one LED and is at an upstream end 28 (shown in Figure 1) of the electronic smoking article 60 so that the heater activation light 27 illuminates a cap which takes on the appearance of a burning coal during a puff. Moreover, the heater activation light 27 can be arranged to be visible to the smoker. In addition, the heater activation light 27 can be utilized

for smoking article system diagnostics. The light 27 can also be configured such that the smoker can activate and/or deactivate the light 27 when desired, such that the light 27 would not activate during smoking if desired.

[0060] The time-period of the electric current supply to the heater 19 may be pre-set depending on the amount of liquid desired to be vaporized. The control circuitry 11 can be programmable and can include an application specific integrated circuit (ASIC). In other embodiments, the control circuitry 11 can include a microprocessor programmed to carry out functions such as heating the capillaries and/or operating the valves.

[0061] As shown in Figures 2, 3 and 4 the electronic smoking article 60 further includes the mouth end insert 20 having at least two off-axis, preferably diverging outlets 21. Preferably, the mouth end insert 20 includes at least two diverging outlets 21. (e.g. 3, 4, 5, or preferably 6 to 8 outlets or more). Preferably, the outlets 21 of the mouth end insert 20 are located at ends of off-axis passages 23 and are angled outwardly in relation to the longitudinal direction of the electronic smoking article 60 (i.e., divergently). As used herein, the term "off-axis" denotes at an angle to the longitudinal direction of the electronic smoking article. Also preferably, the mouth end insert (or flow guide) 20 includes outlets uniformly distributed around the mouth end insert 20 so as to substantially uniformly distribute aerosol in a smoker's mouth during use. Thus, as the aerosol passes into a smoker's mouth, the aerosol enters the mouth and moves in different directions so as to provide a full mouth feel as compared to electronic smoking articles having an on-axis single orifice which directs the aerosol to a single location in a smoker's mouth.

[0062] In addition, the outlets 21 and off-axis passages 23 are arranged such that droplets of unaerosolized liquid material carried in the aerosol impact interior surfaces of the mouth end insert 20 and/or interior surfaces of the off-axis passages 23 such that the droplets are removed or broken apart. In the preferred embodiment, the outlets 21 of the mouth end insert 20 are located at the ends of the off-axis passages 23 and are angled at 5 to 60° with respect to the central longitudinal axis of the electronic smoking article 60 so as to more completely distribute aerosol throughout a mouth of a smoker during use and to remove droplets.

[0063] Preferably, each outlet 21 has a diameter of about 0.015 inch to about 0.090 inch (e.g., about 0.020 inch to about 0.040 inch or about 0.028 inch to about 0.038 inch). The size of the outlets 21 and off-axis passages 23 along with the number of outlets 21 can be selected to adjust the resistance to draw (RTD) of the electronic smoking article 60, if desired.

[0064] Preferably, the electronic smoking article 60 is about the same size as a conventional smoking article. In some embodiments, the electronic smoking article 60 can be about 80 mm to about 110 mm long, preferably about 80 mm to about 100 mm long and about 7 mm to about 8 mm in diameter. For example, in an embodiment, the electronic smoking article is about 84 mm long and has a diameter of about 7.8 mm.

[0065] The outer cylindrical housing 22 of the electronic smoking article 60 may be formed of any suitable material or combination of materials. Preferably, the outer cylindrical housing 22 is formed at least partially of metal and is part of the electrical circuit.

[0066] In the embodiment shown in Figure 2, at least a portion of the outer cylindrical housing 22 can be elastomeric so as to allow a smoker to squeeze the housing 22 and the reservoir 14 during smoking to release liquid material therefrom and activate the heater 19. Thus, the outer cylindrical housing 22 can be formed of a variety of materials including plastics, rubber and combinations thereof. In an embodiment, the outer cylindrical housing 22 is formed of silicone. The outer cylindrical housing 22 can be any suitable color and/or can include graphics or other indicia printed thereon.

[0067] Preferably, the liquid aerosol formulation for use in each of the electronic smoking articles 60 described herein includes at least one aerosol former, water, a nicotine source, and at least one acid.

[0068] In the preferred embodiment, the at least one aerosol former is selected from the group consisting of propylene glycol, glycerin and combinations thereof. Preferably, the at least one aerosol former is included in an amount ranging from about 40% by weight based on the weight of the liquid formulation to about 90% by weight based on the weight of the liquid formulation (e.g., about 50% to about 80%, about 55% to about 75% or about 60% to about 70%). Moreover, in one embodiment, the liquid formulation can include propylene glycol and glycerin included in a weight ratio of about 3:2.

[0069] Preferably, the liquid formulation also includes water. Water can be included in an amount ranging from about 5% by weight based on the weight of the liquid formulation to about 40% by weight based on the weight of the liquid formulation, more preferably in an amount ranging from about 10% by weight based on the weight of the liquid formulation to about 15% by weight based on the weight of the liquid formulation.

[0070] The liquid aerosol formulation optionally includes at least one flavorant in an amount ranging from about 0.2% to about 15% by weight (e.g., about 1% to about 12%, about 2% to about 10%, or about 5% to about 8%). The at least one flavorant can be a natural flavorant or an artificial flavorant. Preferably, the at least one flavorant is selected from the

group consisting of tobacco flavor, menthol, wintergreen, peppermint, herb flavors, fruit flavors, nut flavors, liquor flavors, and combinations thereof.

[0071] Also preferably, the liquid aerosol formulation includes an acid having a melting point and/or a boiling point of at least about 150°C. For example, the acid can have a melting point and/or a boiling point ranging from about 150°C to about 300°C, more preferably about 150°C to about 250°C (e.g., about 160°C to about 240°C, about 170°C to about 230°C, about 180°C to about 220°C or about 190°C to about 210°C). By including an acid having a melting point and/or a boiling point within this range, the acid may volatilize when heated by heater elements of electronic smoking articles as previously described. In an embodiment utilizing a heater coil and a wick, the heater coil may reach an operating temperature at or about 300° C.

[0072] Also preferably, the acid is included in the liquid aerosol formulation in an amount sufficient to reduce the pH of the liquid aerosol formulation to a pH ranging from about 4 to about 8, more preferably about 5 to about 7 or about 5.5 to about 6.5. Moreover, the acid is preferably condensable at ambient temperature.

[0073] Suitable acids for use in the liquid aerosol formulation include, without limitation, succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof. Preferably, the acid is included in an amount ranging from about 0.1% by weight to about 15% by weight (e.g., about 1% to about 12%, about 2% to about 10%, about 3% to about 9% or about 4% to about 8%).

[0074] The amount of acid added to the liquid aerosol formulation may depend on the strength of the acid and the amount needed to adjust the pH of the liquid aerosol formulation to the desired range. If too much acid is added, essentially all of the available nicotine will be protonated and will enter the particulate phase of the aerosol, leaving very little unprotonated nicotine in the gas phase of the aerosol. The resultant aerosol may not produce sufficient levels of sensory response in terms of throat harshness to meet preferences of the more usual smoker of lit-end cigarettes. In contrast, if too little acid is added, a larger amount of nicotine will remain unprotonated and in the gas phase of the aerosol, such that the smoker will experience increased throat harshness. With liquid aerosol formulations of nicotine content above approximately 2% by weight, and in the absence of addition of an acid according to the teachings herein, perceived throat harshness may approach levels which render the aerosol as unpleasant to inhale, and with liquid formulations of nicotine content above approximately 4% by weight, and in the absence of an acid according to the teachings

herein, perceived throat harshness may approach levels rendering the aerosol uninhalable. With the addition of an acid according to the teachings herein, perceived throat harshness is maintained at desirable levels, akin to that experienced with lit-end cigarettes.

[0075] Preferably, the liquid aerosol formulation also includes at least one nicotine source. The nicotine is included in the liquid aerosol formulation in an amount ranging from about 1% by weight to about 10% by weight (e.g., about 2% to about 9%, about 2% to about 8%, about 2% to about 6%).

[0076] In one embodiment, the nicotine source can comprise molecular (unprotonated) nicotine. Typically, molecular nicotine in an aqueous solution has a pH of about 9 to about 10. Thus, the acid would need to be added in an amount sufficient to reduce the pH to about 4 to about 8. In an embodiment, molecular (unprotonated) nicotine is added in liquid form.

[0077] In an alternative embodiment, the nicotine source can comprise one or more nicotine salts, which can be added to a formulation to provide both the nicotine and the acid. The nicotine salt can be a salt of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof. A preferred nicotine-acid salt is nicotine bitartrate.

[0078] When vaporized in the electronic smoking article, the liquid aerosol formulation is capable of forming an aerosol having a particulate phase and a gas phase. Preferably, the particulate phase contains protonated nicotine and the gas phase contains unprotonated nicotine. Also preferably, the majority of nicotine is protonated and in the particulate phase, while a minority amount of nicotine is contained in the gas phase. Once the liquid aerosol formulation has been vaporized, the vapor condenses, nicotine is protonated and particles including the protonated nicotine are formed. A minor amount of the nicotine remains unprotonated and stays in the gas phase of the newly generated aerosol. Preferably, because of the addition the acid, about 0.1 to about 1.0% of the total nicotine content of the aerosol is believed to be unprotonated (e.g., about 0.2% to about 0.7% or about 0.3% to about 0.5%), while the remainder of the available nicotine is believed to be delivered in a protonated (charged) form and in the particulate phase. Preferably, the particulate phase includes particles ranging in size from about 0.2 micron to about 2 microns.

[0079] Not wishing to be bound by theory, it is believed that the addition of an acid having the desired range of melting point and/or boiling point as taught herein allows the acid to initially enter the initial, not fully developed aerosol-vapor system when the liquid is vaporized by the heater of an electronic smoking article. The acid survives the heating, and

remains available to protonate nicotine so that most, if not almost all, of the nicotine remains and/or enters the particulate phase as the aerosol develops. As with an aerosol produced by a lit end cigarette, the initial gas phase nicotine content of the electronically produced aerosol is quite low, preferably in the range of about 0.1 to 1.0% by weight of the total nicotine content of the aerosol, more preferably in the range of about 0.1 to 0.5% by weight of the total nicotine content of the aerosol. Additionally, the nicotine residing in the particulate phase is predominantly protonated and therefore charged and mostly unavailable for transfer into the gas phase of the aerosol.

[0080] Furthermore, the acid may be selected and its concentration may be set sufficient to maintain the aforementioned, desired low levels of gas phase nicotine, even at the more elevated nicotine content levels in the liquid formulation. Adult smokers of lit end cigarettes have reported that they, when smoking the more usual, commercially available, electronic smoking articles, did not experience the perceived warmth in the chest that they expect from inhaling cigarette smoke. These prior electronic smoking articles tended to have e-liquid formulations with low levels of nicotine content, generally about 2% or less. To the adult cigarette smoker, these prior electronic smoking articles lacked an important, pleasurable sensory response of a cigarette smoking experience – perceived warmth in the chest. However, prior electronic smoking articles having e-liquid formulations with higher levels of nicotine content, above about 2%, but generally about 3% or 4% by weight, tended to provide more of the desired perceived warmth in the chest, but heretofore, the aerosols produced unacceptably high levels of perceived harshness in the throat. Upon investigation, it has been found that the gas phase nicotine content of the aerosols constituted about 3 to 4% of the total nicotine content of the aerosols.

[0081] By preparing a liquid formulation comprising nicotine levels greater than 2% or more by weight, more preferably in range of 2% to about 6% by weight, together with an addition of an acid to the liquid formulation in accordance with the teachings herein, the perceived sensory benefits associated with the higher nicotine levels is achieved (warmth in the chest), while also avoiding the sensory deficits previously associated with higher nicotine levels (excessive harshness in the throat), thereby providing adult cigarette smokers an electronic smoking article that provides a sensorially pleasant smoking experience, including a low to moderate harshness response in the throat and a perceived warmth in the chest.

[0082] With the improved liquid formulation, much of the nicotine in the particulate phase is protonated by the presence of the acid, and any nicotine that is removed from the gas phase by absorption in the throat is not readily replaced by nicotine from the particulate

phase. Instead, the protonated nicotine remains in the particulate phase and is not allowed to elevate the harshness response to unacceptable levels. An aerosol produced according to the teachings herein provides enjoyable sensations from low to mild harshness, generally within the expectations of smokers of lit end cigarettes, even with liquid formulations of elevated nicotine content.

[0083] In terms of smoking enjoyment, enjoyable sensations are experienced at low to mild levels of throat harshness whereas unenjoyable and potentially unpleasant sensations are perceived at high to extreme levels of throat harshness.

[0084] To determine the amount of nicotine in the gas phase per puff, a test electronic smoking article including a liquid aerosol formulation as described herein was compared to a control electronic smoking article with a liquid aerosol formulation not including an acid using a gas chromatography/mass spectrometer (GC/MS). The control electronic smoking article formed an aerosol using a liquid aerosol formulation including 6% nicotine and 94% of a 4:1 mixture of glycerin and water, and no acid. The test electronic smoking article formed an aerosol using a liquid aerosol formulation including 6% nicotine, 89% of a 4:1 mixture of glycerin to water, and 5% levulinic acid. Each electronic smoking article was tested over 49 puffs. To determine the nicotine content in the gas phase, the gas vapor was collected behind a Cambridge pad. The results of the test are shown in Figure 5. As shown, the test electronic smoking article provided less nicotine per puff in the gas phase as compared to the control electronic smoking article.

[0085] Unexpectedly, as shown in Figure 5, the addition of an acid to the liquid aerosol formulation reduces gas phase nicotine. While not wishing to be bound by theory, it is believed that adding an acid to the liquid aerosol formulation to form a liquid aerosol formulation having a pH ranging from about 4 to about 8 results in an aerosol containing a majority amount of protonated nicotine in the particulate phase and a minority amount of unprotonated nicotine, which is maintained in the gas phase of the aerosol.

[0086] Advantageously, the addition of tartaric acid (and/or nicotine salt thereof) reduces throat harshness during both inhalation and exhalation. It has been found that use of tartaric acid (and/or nicotine salt thereof), according to the teachings herein, provides little to no harshness to the throat upon exhalation, which is a desirable attribute in terms of sensory response.

[0087] In one embodiment, the liquid aerosol formulation can also include ammonia or ammonia compounds in an amount sufficient to further reduce the pH of the liquid aerosol formulation by about 1 to 2 pH units. The addition of ammonia or ammonia compounds may

prevent or reduce the formation of char at the heater without affecting the harshness in the throat or warmth in the chest.

[0088] When the word "about" is used in this specification in connection with a numerical value, it is intended that the associated numerical value include a tolerance of $\pm 10\%$ around the stated numerical value. Moreover, when reference is made to percentages in this specification, it is intended that those percentages are based on weight, i.e., weight percentages. The expression "up to" includes amounts of zero to the expressed upper limit and all values therebetween. When ranges are specified, the range includes all values therebetween such as increments of 0.1%.

[0089] Moreover, when the words "generally" and "substantially" are used in connection with geometric shapes, it is intended that precision of the geometric shape is not required but that latitude for the shape is within the scope of the disclosure. Although the tubular elements of the embodiments are preferably cylindrical, other tubular cross-sectional forms are contemplated, such as square, rectangular, oval, triangular and others. When used with geometric terms, the words "generally" and "substantially" are intended to encompass not only features which meet the strict definitions but also features which fairly approximate the strict definitions.

[0090] It will now be apparent that a new, improved, and nonobvious electronic smoking article, liquid aerosol formulation and method has been described in this specification with sufficient particularity as to be understood by one of ordinary skill in the art. Moreover, it will be apparent to those skilled in the art that numerous modifications, variations, substitutions, and equivalents exist for features of the electronic smoking article, liquid aerosol formulation and method which do not materially depart from the spirit and scope of the invention. Accordingly, it is expressly intended that all such modifications, variations, substitutions, and equivalents which fall within the spirit and scope of the invention as defined by the appended claims shall be embraced by the appended claims.

We Claim:

1. A liquid aerosol formulation operative in an electronic smoking article having a heater operating temperature comprising:
 - an aerosol former;
 - water in an amount of 0% to about 40% by weight based on the weight of the liquid aerosol formulation;
 - nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation; and
 - an acid having a melting point and/or a boiling point of at least about 150°C and such that the acid volatilizes at the heater operating temperature and is condensable at ambient temperatures, the at least one acid being included in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8;wherein the liquid aerosol formulation forms an aerosol having a particulate phase and a gas phase when heated during operation of the electronic smoking article, the particulate phase containing protonated nicotine and the gas phase containing unprotonated nicotine, the gas phase nicotine content of the aerosol being less than about 1% of a total nicotine content of the aerosol.
2. The liquid aerosol formulation of Claim 1, further comprising at least one flavorant in an amount ranging from about 0.2% to about 15% by weight.
3. The liquid aerosol formulation of Claim 1, wherein the aerosol former is selected from the group consisting of propylene glycol, glycerin and combinations thereof.
4. The liquid aerosol formulation of Claim 3, wherein the aerosol former is included in an amount ranging from about 40% by weight to about 90% by weight.
5. The liquid aerosol formulation of Claim 1, wherein the acid has a boiling point ranging from about 150°C to about 250°C.
6. The liquid aerosol formulation of Claim 1, wherein the acid has a melting point ranging from about 150°C to about 250°C.

7. The liquid aerosol formulation of Claim 3, wherein the liquid formulation comprises glycerin and propylene glycol in a ratio of about 2:3 or greater.
8. The liquid aerosol formulation of Claim 1, wherein nicotine is included in an amount ranging from about 2 % by weight to about 10% by weight.
9. The liquid aerosol formulation of Claim 1, wherein the particulate phase comprises particles ranging in size from about 0.2 micron to about 2 microns.
10. The liquid aerosol formulation of Claim 1, wherein the acid is included in an amount ranging from about 0.1% by weight to about 15% by weight.
11. An electronic smoking article operable to produce an aerosol which substantially replicates a sensory experience of smoking a lit-end cigarette, the electronic smoking article comprising:
 - a heater;
 - a liquid aerosol formulation, the heater operable to volatilize the liquid aerosol formulation and form an aerosol, the liquid aerosol formulation comprising:
 - an aerosol former;
 - water in an amount of 0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation;
 - nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation; and
 - an acid in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8,
 - wherein the liquid aerosol formulation is capable of forming the aerosol having a particulate phase and a gas phase when heated by the heater, the particulate phase containing protonated nicotine and the gas phase containing unprotonated nicotine, and the aerosol having a majority amount of the protonated nicotine and a minority amount of the unprotonated nicotine.
12. The electronic smoking article of Claim 11, wherein the sensory experience includes a perception of chest warmth and moderate throat harshness during a puff.

13. The electronic smoking article of Claim 11, wherein the heater comprises a capillary tube in fluid communication with a reservoir containing the liquid aerosol formulation.

14. The electronic smoking article of Claim 13, wherein the reservoir is pressurized and comprises a mechanically or electrically operated valve at an outlet of the reservoir.

15. The electronic smoking article of Claim 13, wherein the reservoir is compressible such that the liquid aerosol formulation is manually pumped to the capillary.

16. The electronic smoking article of Claim 11, wherein the heater is a coil heater in communication with a filamentary wick which draws the liquid aerosol formulation from a reservoir via capillary action.

17. The electronic smoking article of Claim 16, wherein the electronic smoking article further comprises:

an outer tube extending in a longitudinal direction;

an inner tube within the outer tube; and

wherein the coil heater is located in the inner tube and the filamentary wick is in communication with the reservoir and surrounded by the coil heater such that the wick delivers the liquid aerosol formulation to the coil heater and the coil heater heats the liquid aerosol formulation to a temperature sufficient to vaporize the liquid aerosol formulation and form the aerosol.

18. A method of replicating a sensory experience of smoking a lit-end cigarette with an electronic smoking article, the method comprising:

heating a liquid aerosol formulation with a heater of the electronic smoking article to form an aerosol, the liquid aerosol formulation comprising:

an aerosol former;

water in an amount of 0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation;

nicotine in an amount of about 2% or more by weight based on the weight of the liquid aerosol formulation; and

an acid in an amount sufficient to provide the liquid aerosol formulation with a pH ranging from about 4 to about 8,

wherein the aerosol has a particulate phase and a gas phase, the particulate phase contains protonated nicotine and the gas phase contains unprotonated nicotine, the unprotonated nicotine being less than about 1% of a total nicotine content of the aerosol.

19. The method of Claim 18, wherein the sensory experience includes a perception of chest warmth and moderate throat harshness during a puff.

20. The method of Claim 18, wherein the acid has a melting point and/or a boiling point of at least about 150°C and such that the acid volatilizes at an operating temperature of the heater and is condensable at ambient temperatures.

21. A method of forming an aerosol with an electronic smoking article, the method comprising:

heating a liquid aerosol formulation to a temperature sufficient to form an aerosol, the liquid aerosol formulation comprising:

an aerosol former;

water in an amount of 0% by weight to about 40% by weight based on the weight of the liquid aerosol formulation;

nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation; and

an acid in an amount sufficient to provide the liquid aerosol formulation a pH ranging from about 4 to about 8,

wherein the acid is operative upon the aerosol so as to reduce an amount of perceived throat harshness by a smoker in comparison to the aerosol being formed upon operation of the electronic smoking article without the acid.

22. The method of Claim 21, wherein the acid comprises tartaric acid in an amount ranging from about 0.1% by weight to about 15% by weight based on the weight of the liquid aerosol formulation.

23. The liquid aerosol formulation of Claim 1, wherein the acid is selected from the group consisting of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof.
24. The liquid aerosol formulation of Claim 1, wherein at least some of the acid and at least some of the nicotine is from a nicotine-acid salt.
25. The liquid aerosol formulation of Claim 24, wherein the nicotine-acid salt comprises nicotine bitartrate.
26. The liquid aerosol formulation of Claim 1, wherein the acid comprises tartaric acid.
27. The method of Claim 21, wherein the liquid aerosol formulation further comprises ammonia or an ammonia containing compound in an amount sufficient to reduce the pH of the liquid aerosol formulation by about 1 to about 2 pH units.
28. The liquid aerosol formulation of Claim 1, further comprising ammonia or an ammonia containing compound in an amount sufficient to reduce the pH of the liquid aerosol formulation by about 1 to about 2 pH units.
29. The liquid aerosol formulation of Claim 1, wherein the water is included in an amount of about 5% by weight to about 40% by weight based on the weight of the liquid aerosol formulation.
30. The liquid aerosol formulation of Claim 1, wherein the water is included in an amount of about 5% to about 15% by weight based on the weight of the liquid aerosol formulation.
31. The liquid aerosol formulation of Claim 1, wherein the liquid aerosol formulation has a pH ranging from about 5.5 to about 8.
32. A method of forming a component of an electronic smoking article, the method comprising:

preparing a liquid aerosol formulation by combining an aerosol former in an amount of at least about 50% by weight based on the weight of the liquid aerosol formulation and water in an amount of about 5% by weight to about 40% by weight based on the weight of the liquid aerosol formulation;

adding nicotine bitartrate in an amount sufficient to establish a nicotine content of at least about 2% by weight to the liquid aerosol formulation; and

filling a reservoir of a component of an electronic smoking article with the liquid aerosol formulation.

33. The liquid aerosol formulation of Claim 1, wherein the acid has a melting point and/or a boiling point of about 150°C to about 300°C.

34. An aerosol produced by heating a liquid aerosol formulation in an electronic smoking article, the liquid aerosol formulation including an acid and including a nicotine in an amount of at least about 2% by weight based on the weight of the liquid aerosol formulation, the aerosol having a gas phase nicotine content of the aerosol of less than 1% of a total nicotine content of the aerosol, wherein the acid is operative upon the aerosol so as to reduce an amount of perceived throat harshness by a smoker in comparison to the aerosol being formed upon operation of the electronic smoking article without the acid.

35. The aerosol of Claim 34, wherein the nicotine content is sufficient to produce a perception of chest warmth associated with smoking a lit end cigarette.

36. The aerosol of Claim 34, wherein the acid comprises tartaric acid, whereby throat harshness is abated during both inhalation and exhalation of the aerosol.

37. The electronic smoking article of Claim 11, wherein the acid is selected from the group consisting of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof.

38. The electronic smoking article of Claim 11, wherein the acid comprises tartaric acid.

39. The method of Claim 18, wherein the acid is selected from the group consisting of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof.

40. The method of Claim 18, wherein the acid comprises tartaric acid.

41. The method of Claim 32, wherein the acid is selected from the group consisting of succinic acid, tartaric acid, sulfuric acid, carbonic acid, malonic acid, tartronic acid, levulinic acid, acetic acid, benzoic acid, adipic acid, gluaric acid, pimelic acid and combinations thereof.

42. The method of Claim 32, wherein the acid comprises tartaric acid.

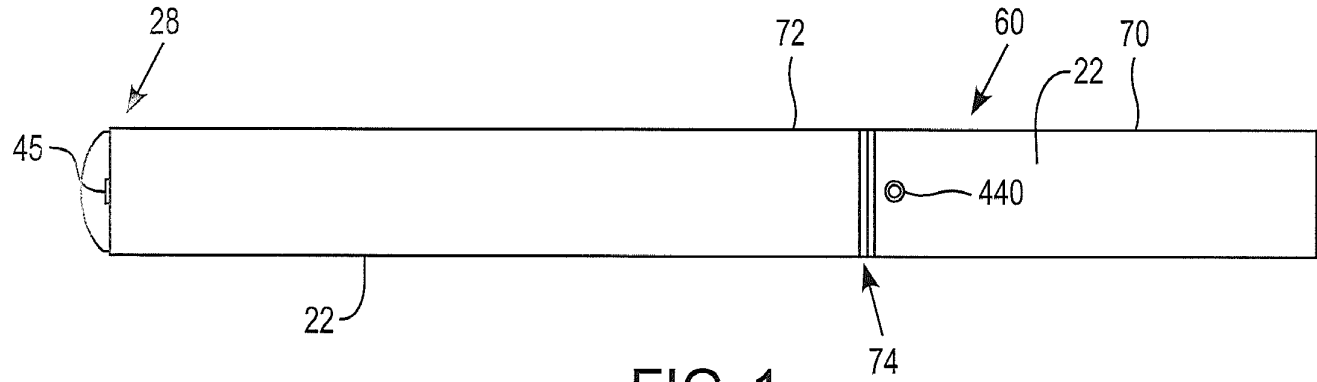


FIG. 1

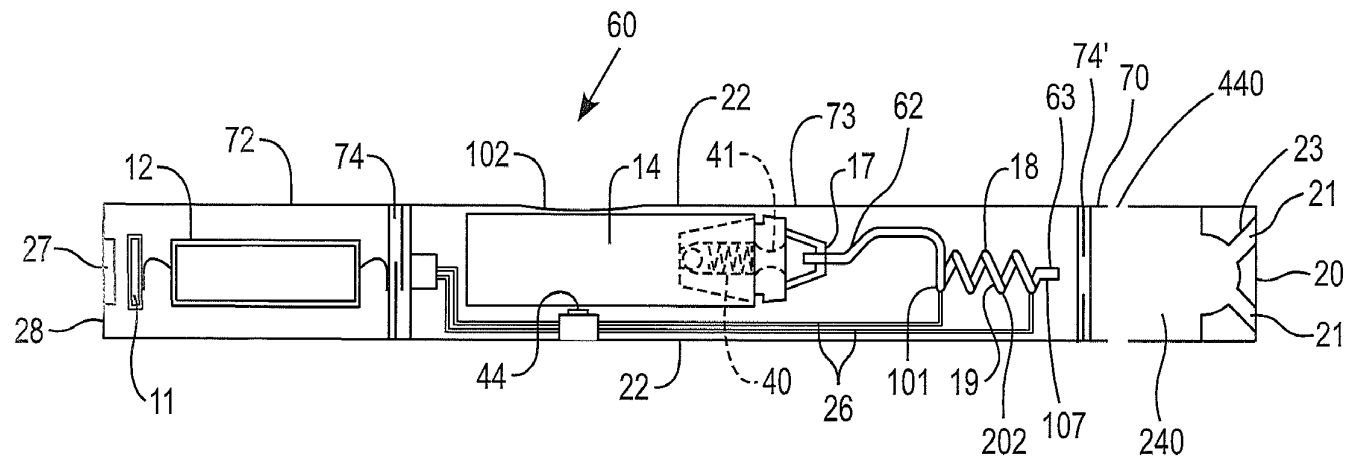


FIG. 2

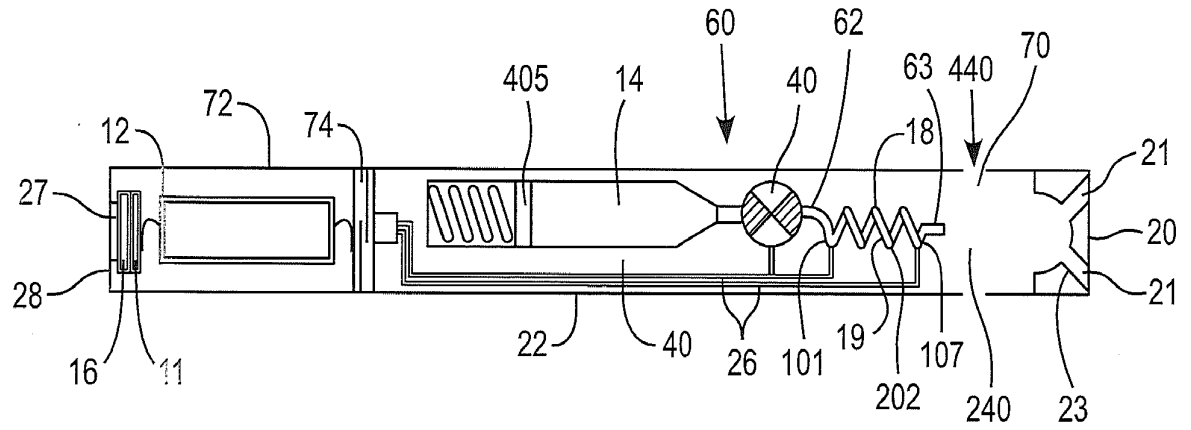


FIG. 3

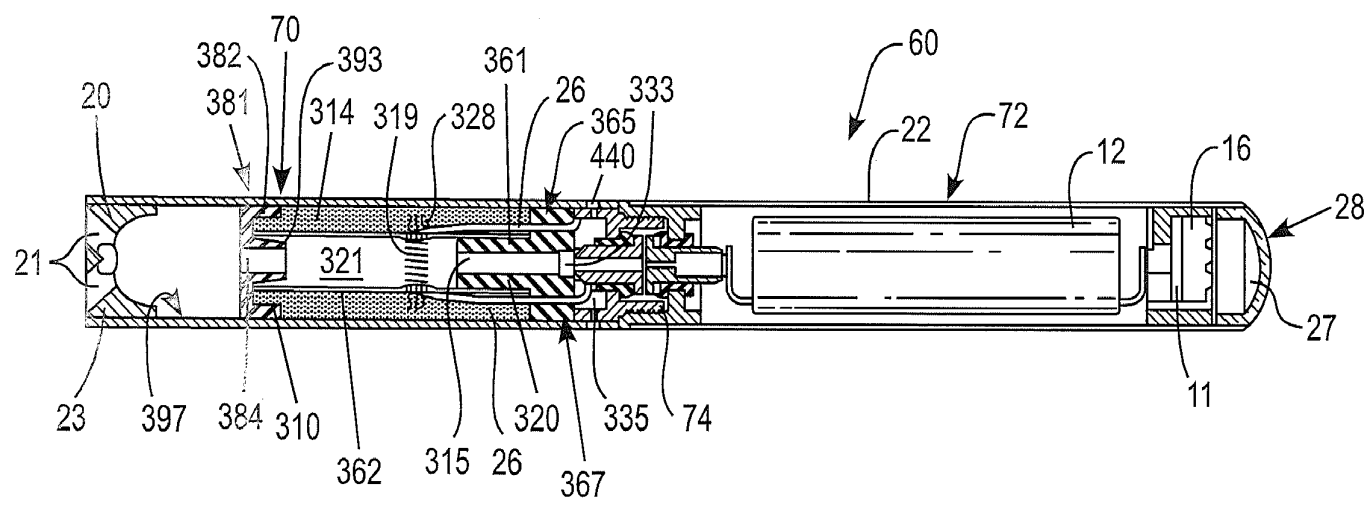


FIG. 4

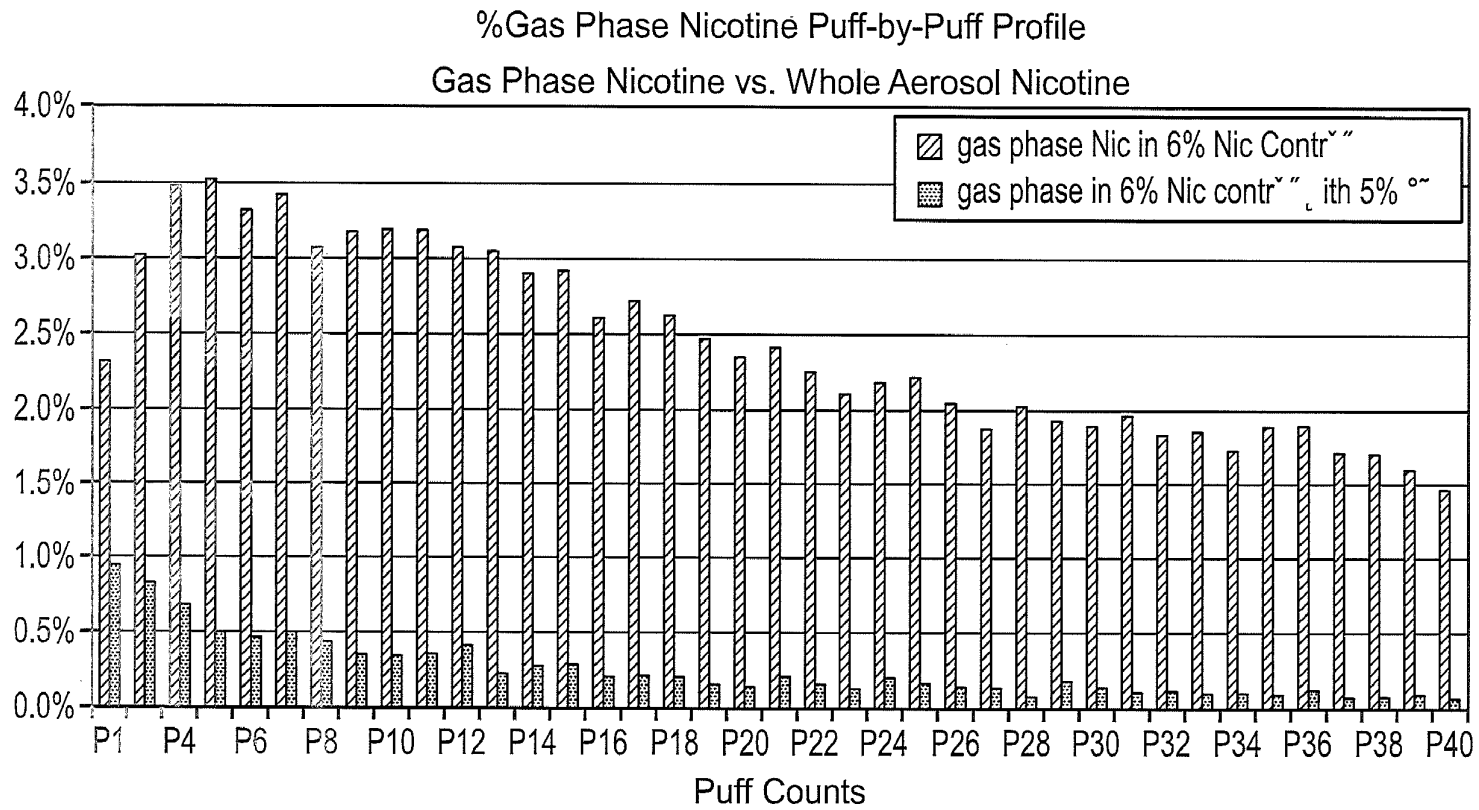


FIG. 5



(11) **EP 2 319 934 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention
of the grant of the patent:
02.09.2015 Bulletin 2015/36

(51) Int. Cl.:
C12N 15/82 (2006.01) **C12N 9/10** (2006.01)
A61K 38/02 (2006.01)

(21) Application number: 10185180.6

(22) Date of filing: 18.03.2003

(54) **GnTIII (UDP-N-acetylglucosamine:Beta -D mannoside Beta (1,4)-N-acetylglucosaminyltransferase III) expression in plants.**

GnTIII (UDP-N-acetylglucosamin:Beta -D mannoside Beta (1,4)-N-acetylglucosaminyltransferase III)
expression in pflanzen

Expression de GnTIII (UDP-N-acétylglucosamine: Beta -D mannoside Beta (1,4)-N-
acétylglucosaminyltransferase III) dans des plantes

(84) Designated Contracting States:
**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HU IE IT LI LU MC NL PT RO SE SI SK TR**

(74) Representative: Sonn & Partner Patentanwälte
Riemergasse 14
1010 Wien (AT)

(30) Priority: 19.03.2002 US 365769 P
26.03.2002 US 368047 P

(56) References cited:
WO-A-01/31045

(43) Date of publication of application:
11.05.2011 Bulletin 2011/19

• LEROUGE P ET AL: "N-glycoprotein biosynthesis in plants: recent developments and future trends", *PLANT MOLECULAR BIOLOGY*, vol. 38, 1998, pages 31-48, XP002140796, ISSN: 0167-4412

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
03715213.9 / 1 485 492

• TANIGUCHI ET AL.: "A glycomic approach to the identification and characterization of glycoprotein function in cells transfected with glycosyltransferase genes", *PROTEOMICS*, vol. 1, 20 January 2001 (2001-01-20), page 239247, XP2638362.

(73) Proprietor: Stichting Dienst Landbouwkundig
Onderzoek
6701 BH Wageningen (NL)

• UMANA P ET AL: "Tetracycline-regulated overexpression of glycosyltransferases in chinese hamster ovary cells", *BIOTECHNOLOGY AND BIOENGINEERING*, WILEY & SONS, HOBOKEN, NJ, US, vol. 65, 1 January 1999 (1999-01-01), pages 542-549, XP002967185, ISSN: 0006-3592, DOI: DOI:10.1002/(SICI)1097-0290(19991205)65:5< 542::AID-BIT7>3.0.CO;2-Z

(72) Inventors:
• Bakker, Hendrikus Antonius Cornelius
30627 Hannover (DE)
• Florack, Dionisius Elisabeth Antonius
6708 MD Wageningen (NL)
• Bosch, Hendrik Jan
6708 NA Wageningen (NL)

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Description

FIELD OF THE INVENTION

5 [0001] The invention relates to expression of a mammalian N-acetylglucosaminyl-transferase III (GnTIII) enzyme in plants and its use in producing glycoproteins with bisected oligosaccharides

BACKGROUND OF THE INVENTION

10 [0002] N-Acetylglucosaminyltransferases (GlcNAc-transferases) are "branching" enzymes that add an N-acetylglucosamine (GlcNAc) residue to one of the mannoses of the trimannosyl core structure of typical N-linked glycans. At least six GlcNAc-transferases are known with little or no sequence homology. Besides different protein structures, these GlcNAc-transferases also have different enzymatic properties and substrate specificity. All are typical type II transmembrane proteins with a cytoplasmic domain, a transmembrane anchor and an extracellular stem region with catalytic domain.

15 [0003] A remarkable GlcNAc-transferase is GlcNAc-transferase III (GnTIII). GnTIII, also known as UDP-N-acetylglucosamine:β-D-mannoside β(1,4)-N-acetylglucosaminyl-transferase III (EC 2.4.1.144), inserts bisecting GlcNAc residues in complex-type N-linked glycans of cellular glycoproteins (for a review see Taniguchi, et al., "A glycomic approach to the identification and characterization of glycoprotein function in cells transfected with glycosyltransferase genes" Proteomics 1:239247, 2001). GnTIII adds the GlcNAc through a β(1,4) linkage to the β-linked mannose of the trimannosyl core structure of the N-linked glycan. GnTIII was first identified in hen oviduct (Narasimhan S., "Control of glycoprotein synthesis. UDP-GlcNAc:glycopeptide β 4-N-acetylglucosaminyltransferase III, an enzyme in hen oviduct which adds GlcNAc in β14 linkage to the β-linked mannose of the trimannosyl core of N-glycosyl oligosaccharides" The Journal of Biological Chemistry 257:10235-10242, 1982) but a high level of activity has also been reported in various types of rat hepatomas, human serum, liver and hepatoma tissues of patients with hepatomas and liver cirrhosis (Ishibashi, et al., "N-acetylglucosaminyltransferase III in human serum and liver and hepatoma tissues: increased activity in liver cirrhosis and hepatoma patients" Clinical Chimica Acta 185:325, 1989; Narishimhan, et al., "Expression of N-acetylglucosaminyltransferase III in hepatic nodules during rat liver carcinogenesis promoted by orotic acid" Journal of Biological Chemistry 263:1273-1281, 1988; Nishikawa, et al., "Determination of N-acetylglucosaminyltransferases III, IV and V in normal and hepatoma tissues of rats" Biochimica et Biophysica Acta 1035:313-318, 1990; Pascale, et al., "Expression of N-acetylglucosaminyltransferase III in hepatic nodules generated by different models of rat liver carcinogenesis" Carcinogenesis 10:961964, 1989). Bisected oligosaccharides on glycoproteins have been implicated in antibody-dependent cellular cytotoxicity (ADCC). ADCC is a lytic attack on antibody-targeted cells and is triggered upon binding of lymphocyte receptors to the constant region (Fc) of antibodies. Controlled expression of GnTIII in recombinant Chinese Hamster Ovary (CHO) production cell lines that lack GnTIII activity resulted in antibodies with bisected oligosaccharides with optimized ADCC activity (Davies, et al., "Expression of GnTIII in a recombinant anti-CD20 CHO production cell line: expression of antibodies with altered glycoforms leads to an increase in ADCC through higher affinity for FcγRIII" Biotechnology and Bioengineering 74:288-294, 2001; Umana, et al., "Engineered glycoforms of an antineuroblastoma IgG1 with optimized antibody-dependent cellular cytotoxic activity" Nature Biotechnology 17:176-180, 1999). The ADCC activity correlated well with the level of Fc region-associated bisected complex oligosaccharides present on the recombinant antibody (Umana, et al., "Engineered glycoforms of an antineuroblastoma IgG1 with optimized antibody-dependent cellular cytotoxic activity" Nature Biotechnology 17:176-180, 1999). Bisecting GlcNAc residues resulting from GnTIII activity affect the conformation of the sugar chains in such a way that other glycosyltransferases such as GlcNAc-transferase II and α1,6-fucosyltransferase, but not β(1,4)-galactosyltransferase, can no longer act (Taniguchi, et al., 2001). Overexpression of GnTIII in CHO cells is lethal.

20 [0004] In contrast to typical mammalian production cell lines such as CHO cells, transgenic plants are generally recognized as a safe production system for therapeutic proteins. Plant glycoproteins, however, differ in oligosaccharide structure with those from mammals in several aspects. They lack terminal galactose and sialic acid, have an additional core xylose and differently linked core fucose (α-1,3) instead of (α-1,6). Like CHO and other pharmaceutical production cell lines they also completely lack bisected oligosaccharides. Plants have the capacity to generate the common core structure, GN2M3GN2 but predominantly M3 GN2 variants are found, indicating removal of terminal GN by hexosaminidases.

25 [0005] Biogenesis of N-linked glycans begins with the synthesis of a lipid linked oligosaccharide moiety (Glc3Man9GlcNAc2-) which is transferred *en bloc* to the nascent polypeptide chain in the endoplasmic reticulum (ER). Through a series of trimming reactions by exoglycosidases in the ER and cis-Golgi compartments the so-called "high mannose" (Man9GlcNAc2 to Man5GlcNAc2) glycans are formed. Subsequently, the formation of complex type glycans starts with the transfer of the first GlcNAc onto Man5GlcNAc2 by GnTI and further trimming by mannosidase II (Mann) to form GlcNAcMan3 GlcNAc2. Complex glycan biosynthesis continues while the glycoprotein is progressing through

the secretory pathway with the transfer in the Golgi apparatus of the second GlcNAc residue by GnTII as well as other monosaccharide residues onto the GlcNAcMan₃GlcNAc₂ under the action of several other glycosyl transferases. Plants and mammals differ with respect to the formation of complex glycans. In plants, complex glycans are characterized by the presence of $\beta(1,2)$ -xylose residues linked to the Man-3 and/or an $\alpha(1,3)$ -fucose residue linked to GlcNAc₁, instead of an $\alpha(1,6)$ -fucose residue linked to the GlcNAc-1 (Lerouge, P., et al., "N-glycoprotein biosynthesis in plants: recent developments and future trends" *Plant Mol Biol* 38:31-48, 1998). Genes encoding the corresponding xylosyl (XylT) and fucosyl (FucT) transferases have been isolated (Stüsser R., "molecular cloning and functional expression of $\beta 1, 2$ -xylosyltransferase cDNA from *Arabidopsis thaliana*" *FEBS Lett.* 472:105-8, 2000; Leiter, H., et al., "Purification, cDNA cloning, and expression of GDP-L-Fuc:Asn-linked GlcNAc α 1,3-fucosyltransferase from mung beans" *J Biol Chem.* 274:21830, 1999). Xylose and fucose epitopes are known to be highly immunogenic and possibly allergenic which may pose a problem when plant are used for the production of therapeutic glycoproteins. Moreover, blood serum of many allergy patients contains IgE directed against these epitopes which make particularly these patients at risk to treatments with xylose and fucose containing recombinant proteins. In addition, this carbohydrate directed IgE in sera might cause false positive reaction in *in vitro* tests using plant extracts since there is evidence that these carbohydrate specific IgE's are not relevant for the allergenic reaction. Plants do not possess $\beta(1,4)$ galactosyltransferases nor $\alpha(2,6)$ sialyltransferases and consequently plant glycans lack the $\beta(1,4)$ galactose and terminal $\alpha(2,6)$ NeuAc residues often found on mammalian glycans (Vitale and Chrispeels, "Transient N-acetylglucosamine in the biosynthesis of phytohemagglutinin: attachment in the Golgi apparatus and removal in protein bodies" *J Cell Biol* 99:133-140, 1984; Lerouge, P., et al., "N-glycoprotein biosynthesis in plants: recent developments and future trends" *Plant Mol Biol* 38:31-48, 1998).

[0006] The final glycan structures are not only determined by the mere presence of enzymes involved in their biosynthesis but to a large extend by the specific sequence of the various enzymatic reactions. The latter is controlled by discrete sequestering and relative position of these enzymes throughout the ER and Golgi, which is mediated by the interaction of determinants of the transferase and specific characteristics of the sub-Golgi compartment for which the transferase is destined. A number of studies using hybrid, molecules have identified that the transmembrane domains of several glycosyltransferases play a central role in their sub-Golgi sorting (Grabenhorst E., et al., *J. Biol. Chem.* 274:36107-36116, 1999; Colley, K., *Glycobiology* 7:1-13, 1997; Munro, S., *Trends Cell Biol.* 8:11-15, 1998; Gleeson P.A., *Histochem. Cell Biol.* 109:517-532, 1998).

[0007] Similar to mammalian production cell lines used in pharmaceutical industry, glycoproteins produced in plants lack GnTIII activity. Plants not only lack GnTIII activity but are completely devoid of GnTIII-like sequences. In addition, plants also lack GnTIV, GnTV and GnTVI sequences and moreover, sialic acid residues. (For an overview of the major glycosylation attributes of commonly used cell expression systems including plants see, Jenkins, et al., "Getting the glycosylation right: implications for the biotechnology industry" *Nature Biotechnology* 14:975-979, 1996). Nevertheless, plants are a very potent production system. Plants are generally accepted as safe and are free of particles infectious to humans. Plant production is easy scalable and N-linked glycosylation can be controlled (Bakker, et al., "Galactose-extended glycans of antibodies produced by transgenic plants" *Proc. Nat. Acad. Sci. USA* 98:2899-2904, 2001).

[0008] Transgenic tobacco plants that produce galactosylated recombinant monoclonal antibodies (Mabs) upon introduction of the human gene for $\beta(1,4)$ -galactosyltransferase have been reported (hGalT; Bakker, et al., "Galactose-extended glycans of antibodies produced by transgenic plants" *Proc. Nat. Acad. Sci. USA* 98:2899-2904, 2001; WO01/31044 and WO01/31045).

[0009] Therapeutic glycoproteins can be improved by altering their glycosylation pattern (Davies, et al., "Expression of GnTIII in a recombinant anti-CD20 CHO production cell line: expression of antibodies with altered glycoforms leads to an increase in ADCC through higher affinity for Fc γ RIII" *Biotechnology and Bioengineering* 74:288-294, 2001; Umana, et al., "Engineered glycoforms of an antineuroblastoma IgG1 with optimized antibody-dependent cellular cytotoxic activity" *Nature Biotechnology* 17:176-180, 1999; Fukuta, et al., "Remodeling of sugar chain structures of human interferon- γ " *Glycobiology* 10:421-430, 2000; Misaizu, et al., "Role of antennary structure of N-linked sugar chains in renal handling of recombinant human erythropoietin" *Blood* 86:4097-4104, 1995; Sburlati, et al., "Synthesis of bisected glycoforms of recombinant IFN- β by overexpression of β -1,4-N-acetylglucosaminyl-transferase III in Chinese Hamster Ovary cells" *Biotechnology Prog.* 14:189-192, 1998). Higher oligosaccharide antennarity of EPO, for example, leads to increased *in vivo* activity due to reduced kidney filtration (Misaizu, et al., "Role of antennary structure of N-linked sugar chains in renal handling of recombinant human erythropoietin" *Blood* 86:4097-4104, 1995). Biosynthesis of such superior glycoforms can be achieved with the "standard" glycosylation machinery of normal production cell lines by two methodologies. The first is by enriching specific glycoforms during purification and the second is by introducing mutations in the polypeptide chain. The latter makes it possible to shift the glycosylation site within the glycoprotein resulting in different glycosylation patterns as the result of differences in accessibility. A complementary route is through genetic engineering of the production cell line itself. New glycosylation patterns can be obtained through expression of glycosyltransferase and glycosidase genes in production cell lines. These genes code for enzymes that either add or remove specific saccharides to and from the glycan of cellular glycoproteins. Several glycosyltransferase genes have been introduced in CHO cells to manipulate glycoform biosynthesis. One of them is GnTIII. Glycosyltransferase GnTIII is involved in branching of the

N-linked glycan and results in bisecting GlcNAc residues. CHO cells and other production cell lines typically lack GnTIII activity (Stanley, P. and C.A. Campbell, "A dominant mutation to ricin resistance in chinese hamster ovary cells induces UDP-GlcNAc: glycopeptide β -4-N-acetylglucosaminyl-transferase III activity" *Journal of Biological Chemistry* 261:13370-13378, 1984). Expression of GnTIII in CHO resulted in bisected complex oligosaccharides as expected but overexpression resulted in growth inhibition and was toxic to cells. Similarly, overexpression of GnTV, another glycosyltransferase that introduces triantennary sugar chains, also resulted in growth inhibition suggesting that this may be a general feature of glycosyltransferase overexpression (Umana, et al., "Engineered glycoforms of an antineuroblastoma IgG1 with optimized antibody-dependent cellular cytotoxic activity" *Nature Biotechnology* 17:176-180, 1999).

[0010] Therefore, there is a need to provide a means for producing glycoprotein in plants with human compatible non-immunogenic bisecting oligosaccharides.

SUMMARY OF THE INVENTION

[0011] The invention relates to a method for producing a plant-derived glycoprotein comprising bisected oligosaccharides, comprising introducing a nucleic acid sequence encoding a mammalian UDP-N- acetylglucosamine: β -D-mannoside β (1,4)-N-acetylglucosaminyltransferase III (GnTIII) and a nucleic acid sequence encoding a heterologous glycoprotein into a plant or portion thereof, and isolating the heterologous glycoprotein. The mammalian GnTIII may comprise the amino acid sequence of SEQ ID NO:2.

[0012] In a specific embodiment, the plant or portion thereof is a plant cell, a whole plant, or a portion thereof, which optionally is selected from the group consisting of leaf, callus, stem, pericarp, protoplast, root, tuber, kernel, endosperm, and embryo. The plant may a tobacco plant.

[0013] In a specific embodiment, the plant or portion thereof further comprises at least one additional non-plant glycosyltransferase that is involved in N-glycan synthesis. The at least one additional non-plant glycosyltransferase may be a mammalian p-1,4 galactosyltransferase.

[0014] Disclosed herein is the expression of a mammalian N-acetylglucosaminyl-transferase III (GnTIII) enzyme in plants and its use in producing glycoproteins with bisected oligosaccharides and increased amount of terminal GlcNAc residues. Also disclosed is a hybrid protein comprising the catalytic site of GnTIII and transmembrane domain of Golgi apparatus and/or endoplasmic reticulum (ER) protein or modified GnTIII comprising ER retention signals and its use in producing glycoproteins with oligosaccharides that lack immunogenic xylose and fucose residues.

[0015] Disclosed herein is a plant host system comprising or expressing a mammalian UDP-Nacetylglucosamine:(β -D-mannoside β (1,4)-Nacetylglucosaminyltransferase (GnTIII) enzyme (nucleotide sequence: SEQ ID NO.: 1, Genbank I.D. number AL022312 (Dunham, I., et al., *Nature* 402:489-495, 1999); protein sequence: SEQ ID NO.: 2, Genbank I.D. number Q09327), wherein said GnTIII inserts bisecting Nacetyl glucosamine (GlcNAc) residues in complex-type N-linked glycans of a glycoprotein present in said plant host system.

[0016] The plant host system further comprises a heterologous glycoprotein or functional fragment thereof comprising bisected oligosaccharide, particularly galactose residues. The GnTIII inserts bisecting N-GlcNAc residues onto said heterologous glycoprotein.

[0017] Disclosed herein is a method for obtaining a plant host system expressing a heterologous glycoprotein comprising bisecting oligosaccharides. The method comprises crossing a plant expressing a heterologous glycoprotein with a plant expressing said GnTIII, harvesting progeny from said crossing and selecting a desired progeny plant expressing said heterologous glycoprotein and expressing mammalian GnTIII. Alternatively, said plant host system may be obtained by introducing into a plant or portion thereof a nucleic acid encoding said mammalian GnTIII and a nucleic acid encoding said heterologous glycoprotein and isolating a plant or portion thereof expressing said heterologous glycoprotein and expressing mammalian GnTIII that is normally not present in plants. Furthermore, Also disclosed is a method for obtaining said heterologous glycoprotein from said plant comprising obtaining a plant host system using either of the procedures described above and further isolating said heterologous glycoprotein.

[0018] In another embodiment, it is contemplated that the plant host system of the present disclosure further comprises a functional mammalian enzyme providing N-glycan biosynthesis that is normally not present in plants thereby, for example, providing the capacity to extend an N-linked glycan by the addition of a galactose as described in WO 01 /21045. In another embodiment, the present disclosure further contemplates a plant host system, wherein said plant host system comprises crossing a plant, said plant comprising a functional protein such as a transporter protein or a enzyme (e.g., a mammalian protein) or functional fragment thereof wherein said protein provides N-glycan biosynthesis, with a plant comprising said mammalian GnTIII. In another embodiment, the present disclosure contemplates harvesting the progeny from said crossing and selecting a desired progeny plant expressing said functional protein such as, for example, a transporter protein or enzyme or functional fragment thereof. In yet another embodiment of the present disclosure it is contemplated that the expressed protein provides N-glycan biosynthesis and the mammalian GnTIII. In still yet another embodiment, the present disclosure contemplates a plant host system, wherein a nucleic acid encoding the GnTIII and a nucleic acid encoding a functional protein (for example, a transporter or an enzyme [e.g., mammalian])

or functional fragment thereof) providing N-glycan biosynthesis and isolating said plant or portion thereof expressing the functional protein or functional fragment thereof providing N-glycan biosynthesis and said mammalian GnTIII. Although the present disclosure is not limited to any particular theory or mechanism, it is believed that such a combination increases galactosylation of a heterologous glycoprotein. Additionally, in one embodiment, it is contemplated that GnTIII and other

5 proteins providing N-glycosylation such as GalT can also be introduced simultaneously via one transformation vector. **[0019]** In one embodiment, the present disclosure contemplates a plant host system comprising expressing said heterologous glycoprotein (wherein, said heterologous glycoprotein has increased galactosylation) and methods for obtaining said plant host cell system and said heterologous glycoprotein. In another embodiment, the plant host cell system may be obtained by either crossing a plant wherein the plant comprises mammalian GnTIII and a functional

10 protein (for example, a transporter or an enzyme [e.g., mammalian] or functional fragment thereof that provides N-glycan biosynthesis not normally found in plants) with a plant comprising a heterologous glycoprotein and, then, selecting said progeny plants. In yet another embodiment, it is contemplated that said heterologous glycoprotein may be obtained by introducing nucleic acid sequences encoding 1) said GnTIII, 2) said functional protein or enzyme providing N-glycan biosynthesis not normally found in plants and 3) said heterologous glycoprotein into said plant or portion thereof and

15 isolating said plant or portion thereof expressing said nucleic acid sequences. In another embodiment of the present disclosure, it is contemplated that the heterologous glycoproteins will be isolated or purified from the plant host systems. **[0020]** In one embodiment of the present disclosure, a hybrid protein is contemplated, wherein the hybrid protein comprises 1) an isolated hybrid protein comprising a catalytic portion of mammalian GnTIII and 2) a transmembrane portion of a protein from, for example, the endoplasmic reticulum or Golgi apparatus of a eukaryotic cell. In another

20 embodiment, the present disclosure also contemplates a modified mammalian GnTIII comprising a retention signal such as KDEL for retention of said GnTIII in the ER. In yet another embodiment, the present disclosure contemplates nucleic acid sequences encoding 1) said hybrid proteins and said modified mammalian GnTIII, 2) vectors comprising said nucleic acid sequences and 3) plant host systems comprising said sequences. In one embodiment, these hybrid proteins and modified GnTIIIs may act to relocalize GnTIII activity in the endoplasmic reticulum (ER) and/or Golgi apparatus. In

25 another embodiment, the present disclosure contemplates methods for obtaining these hybrid proteins and modified GnTIII proteins by, for example, introducing sequences encoding said hybrid proteins or modified GnTIIIs into a plant or portion thereof. Although the present disclosure is not limited to any particular theory or mechanism, it is believed that as a result of such relocalization, bisecting GlcNAc is introduced earlier in the N-glycan biosynthesis sequence of reactions thereby preventing subsequent enzymatic reactions and, as a consequence, a heterologous protein expressed in a plant host system (for example, the plant host system of the present invention) will lack xylose and fucose and have increased amount of terminal GlcNAc. Accordingly, one embodiment of the present disclosure contemplates a method to provide a plant host system expressing a heterologous glycoprotein (said plant host system having the capacity to extend an N-linked glycan with galactose) comprising crossing a plant comprising said 1) hybrid protein or said modified GnTIII with a plant comprising said heterologous protein and 2) selecting said desired progeny. In another

30 embodiment, the present disclosure contemplates introducing into a plant or portion thereof a nucleic acid sequence encoding 1) said modified GnTIII or said hybrid protein and said heterologous glycoprotein and 2) isolating said plant or portion thereof expressing a heterologous glycoprotein with the capacity to extend and N-linked glycan with galactose. In yet another embodiment, the present disclosure contemplates a method for obtaining said desired heterologous glycoprotein, said method comprising isolating said glycoprotein from said plant or portion thereof.

40 **[0021]** In one embodiment, the present disclosure contemplates that the plant-derived glycoprotein or functional fragment thereof may be used for the production of a pharmaceutical composition (for example, an antibody, a hormone, a vaccine antigen, an enzyme, or the like). In another embodiment, the present disclosure contemplates a pharmaceutical composition comprising a glycoprotein or functional fragment thereof is now also provided.

[0022] In one embodiment, the present disclosure contemplates variants or mutants of GnTIII. The terms "variant" and

45 "mutant" when used in reference to a polypeptide refer to an amino acid sequence that differs by one or more amino acids from another, usually related, polypeptide. In another embodiment, the present disclosure contemplates variants that have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties. One type of conservative amino acid substitutions refers to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups are: valine (V) -leucine (L) -isoleucine (I), phenylalanine (F) -tyrosine (Y), lysine (K) -arginine (R),

50 alanine (A) -valine (V), and asparagine (N) -glutamine (Q).

[0023] In yet another embodiment, the present disclosure contemplates variants that have "non-conservative" changes (e.g., replacement of a glycine with a tryptophan). Similar minor variations may also include amino acid deletions or insertions (i.e., additions), or both. Guidance in determining which and how many amino acid residues may be substituted,

inserted or deleted without abolishing biological activity may be found using computer programs well known in the art, for example, DNASTar software. Variants can be tested in functional assays. For both conservative and non-conservative variants, preferred variants have less than 10 %, preferably less than 5 % and, still more preferably, less than 2 % changes (whether substitutions, deletions, and so on).

5 **[0024]** In one embodiment, the present disclosure contemplates a plant host (cell) system, comprising a mammalian UDP-N-acetylglucosamine: β -D mannoside β (1,4)-N-acetylglucosaminyltransferase (GnTIII) enzyme (or portion or variant thereof, wherein said GnTIII inserts bisecting N-acetyl glucosamine (GlcNAc) residues in complex-type N-linked glycans of a glycoprotein present in said plant host system). In another embodiment, the present disclosure contemplates the plant host, wherein said GnTIII is a human GnTIII. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said system is a portion of a plant. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said system is a portion of a plant selected from the group consisting of a cell, leaf, embryo, callus, stem, pericarp, protoplast, root, tuber, kernel, endosperm and embryo. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said system is a whole plant. In yet another < 1 embodiment, the present disclosure contemplates the plant host system, further comprising a heterologous glycoprotein (or functional fragment thereof). In yet another embodiment, the present disclosure contemplates the plant host system, wherein said heterologous glycoprotein protein comprises an antibody, or fragment (e.g. Fc, Fv, Fab, Fab₂) thereof. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said heterologous glycoprotein or functional fragment thereof comprises bisected oligosaccharides. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said heterologous glycoprotein (or functional fragment thereof) comprises bisected glycans with galactose residues. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said plant is a tobacco plant. In yet another embodiment, the present disclosure contemplates the plant host system, which further comprises a functional protein selected from a group consisting of a transporter or a (mammalian) enzyme (or functional fragment thereof) providing N-glycan biosynthesis. In yet another embodiment, the present disclosure contemplates the plant host system, wherein said enzyme is a (human) β -1,4 galactosyltransferase. In yet another embodiment, the present disclosure contemplates the plant host system, which further comprises a heterologous glycoprotein, having an increased number of galactose residues. In yet another embodiment, the present disclosure contemplates a plant host system comprising a nucleic acid sequence encoding a mammalian GnTIII protein. In yet another embodiment, the present disclosure contemplates a plant host system comprising a vector comprising a nucleic acid sequence encoding a mammalian GnTIII protein. In yet another embodiment, the present disclosure contemplates the plant host, which further comprises a nucleic acid sequence encoding a functional protein selected from a group consisting of a transporter or a (mammalian) enzyme (or functional fragment thereof) providing N-glycan biosynthesis.

[0025] In one embodiment, the present disclosure contemplates a method (for obtaining a plant host system expressing a heterologous glycoprotein having bisected oligosaccharides) comprising a) crossing a plant expressing a heterologous glycoprotein with a, b) harvesting progeny from said crossing and c) selecting a desired progeny plant (expressing said heterologous glycoprotein and expressing a mammalian GnTIII that is normally not present in plants). In another embodiment, the present disclosure contemplates this method, wherein said desired progeny plant expresses said heterologous glycoprotein protein having bisected oligosaccharides. In yet another embodiment, the present disclosure contemplates this method, wherein said plant host system is a transgenic plant.

40 **[0026]** In one embodiment, the present disclosure contemplates a method for obtaining a heterologous glycoprotein having bisected oligosaccharides comprising a) introducing a nucleic acid sequence encoding GnTIII that is normally not present in plant into a plant host system and a nucleic acid sequence encoding a heterologous glycoprotein and b) isolating said heterologous glycoprotein. In another embodiment, the present disclosure contemplates this method, wherein said nucleic acid sequences are introduced into a plant cell and said plant cell is regenerated into a plant. In yet another embodiment, the present disclosure contemplates the same method, wherein said nucleic acid sequences are introduced into a plant host system by transforming said plant host system with a vector comprising a nucleic acid sequence encoding GnTIII that is normally not present in plant into a plant and a nucleic acid sequence encoding a heterologous glycoprotein. In yet another embodiment, the present disclosure contemplates the method, wherein said nucleic acid sequences are introduced into a plant host system by transforming said plant host system with a vector comprising a nucleic acid sequence encoding GnTIII that is normally not present in plant into a plant and a nucleic acid sequence encoding a heterologous glycoprotein. In yet another embodiment, the present disclosure contemplates the method, wherein said nucleic acid sequences are introduced into a plant host system by transforming said plant with a vector comprising a nucleic acid sequence encoding GnTIII that is normally not present in plant into a plant host system and vector comprising a nucleic acid sequence encoding a heterologous glycoprotein. In yet another embodiment, the present disclosure contemplates a method for obtaining a heterologous glycoprotein having bisected oligosaccharides comprising cultivating the regenerated plant.

[0027] In one embodiment, the present disclosure contemplates a method for obtaining a desired glycoprotein (or functional fragment thereof) comprising a) cultivating the plant host system (until said plant has reached a harvestable

stage) and b) harvesting said plant (and fractionating to obtain fractionated plant material and c) at least partly isolating said glycoprotein from said fractionated plant material). In another embodiment, the present disclosure contemplates a plant obtainable by the contemplated method.

[0028] In one embodiment, the present disclosure contemplates a method for obtaining a plant host system comprising a functional protein selected from a group consisting of a transporter or a (mammalian) enzyme or functional fragment thereof providing N-glycan biosynthesis and a mammalian GnTIII comprising crossing a plant comprising a functional protein such as a transporter or a (mammalian) enzyme or functional fragment thereof providing N-glycan biosynthesis with a plant disclosure harvesting progeny from said crossing and selecting a desired progeny plant expressing said functional protein such as a transporter or a (mammalian) enzyme or functional fragment thereof providing N-glycan biosynthesis and said mammalian GnTIII. In another embodiment, the present disclosure contemplates a transgenic plant obtained according to the contemplated.

[0029] In one embodiment, the present disclosure contemplates a method for increasing galactosylation of a heterologous glycoprotein expressed in a plant host system comprising introducing a nucleic acid sequence encoding GnTIII and a sequence selected from a group consisting of sequences that encode a transporter or a (mammalian) enzyme or functional fragment not normally present in a plant into said plant host system expressing said heterologous glycoprotein and isolating said glycoprotein.

[0030] In one embodiment, the present disclosure contemplates a plant derived glycoprotein comprising bisected oligosaccharides.

[0031] In one embodiment, the present disclosure contemplates the use of a plant host system disclosed herein to produce a desired glycoprotein or functional fragment thereof. In another embodiment, the present disclosure contemplates that said glycoprotein or functional fragment thereof comprises bisected oligosaccharides. In yet another embodiment, the present disclosure contemplates a plant-derived glycoprotein or functional fragment thereof obtained by a method disclosed herein. In yet another embodiment, the present disclosure contemplates a glycoprotein or functional fragment thereof disclosed herein for the production of a pharmaceutical composition. In yet another embodiment, the present disclosure contemplates a composition comprising a glycoprotein or functional fragment thereof as disclosed herein.

[0032] In one embodiment, the present disclosure contemplates an isolated hybrid protein comprising an active site of GnTIII and a transmembrane region of a protein, said protein residing in endoplasmic reticulum or Golgi apparatus of a eukaryotic cell. In another embodiment, the present disclosure contemplates the protein of the present disclosure, wherein said protein residing in endoplasmic reticulum or Golgi apparatus of a eukaryotic cell is an enzyme. In yet another embodiment, the present disclosure contemplates the protein of the present disclosure, wherein said protein residing in endoplasmic reticulum or Golgi apparatus of a eukaryotic cell is a glycosyltransferase. In yet another embodiment, the present disclosure contemplates the protein of the present disclosure, wherein said protein residing in endoplasmic reticulum or Golgi apparatus of a eukaryotic cell is a glycosyltransferase selected from the group consisting of a mannosidase, mannosidase II, GnTI, GnTII, Xy1T and FucT. In yet another embodiment, the present disclosure contemplates the protein of the present disclosure, wherein said protein residing in endoplasmic reticulum or Golgi apparatus of a eukaryotic cell is a plant protein. In yet another embodiment, the present disclosure contemplates an isolated nucleic acid sequence encoding the protein of the present disclosure. In yet another embodiment, the present invention contemplates a vector comprising the isolated nucleic acid sequence of the present disclosure. In yet another embodiment, the present disclosure contemplates a plant comprising the isolated nucleic acid sequence of the present disclosure. In yet another embodiment, the present disclosure contemplates the plant(s) of the present disclosure which further comprises a nucleic acid sequence encoding a heterologous glycoprotein.

[0033] In one embodiment, the present disclosure contemplates a method (for providing a transgenic plant capable of expressing a heterologous glycoprotein with the capacity to extend an N-linked glycan with galactose) comprising a) crossing a transgenic plant with a plant of the present disclosure, b) harvesting progeny from said crossing and c) selecting a desired progeny plant (expressing said recombinant protein and expressing a functional (mammalian) enzyme involved in (mammalian) N-glycan biosynthesis that is normally not present in plants).

[0034] In one embodiment, the present disclosure contemplates a method for providing a transgenic plant capable of expressing a heterologous glycoprotein with the capacity to extend an N-linked glycan with galactose comprising introducing the nucleic acid sequence of the present disclosure and a nucleic acid sequence encoding said heterologous glycoprotein.

[0035] In one embodiment, the present disclosure contemplates a method, comprising: a) providing: i) a plant cell, and ii) an expression vector comprising nucleic acid encoding a GnTIII enzyme; and b) introducing said expression vector into said plant cell under conditions such that said enzyme is expressed. In another embodiment, the present disclosure contemplates the method, wherein said nucleic acid encoding a GnTIII comprises the nucleic acid sequence of SEQ ID NO:1.

[0036] In one embodiment, the present disclosure contemplates a method, comprising: a) providing: i) a plant cell, ii) a first expression vector comprising nucleic acid encoding a GnTIII enzyme, and iii) a second expression vector com-

prising nucleic acid encoding a heterologous glycoprotein; and b) introducing said first and second expression vectors into said plant cell under conditions such that said hybrid enzyme and said heterologous protein are expressed. In another embodiment, the present disclosure contemplates the method, wherein said heterologous protein is an antibody or antibody fragment.

[0037] In one embodiment, the present disclosure contemplates A method, comprising: a) providing: i) a first plant comprising a first expression vector, said first vector comprising nucleic acid encoding a GNTIII enzyme, and ii) a second plant comprising a second expression vector, said second vector comprising nucleic acid encoding a heterologous protein; and b) crossing said first plant and said second plant to produce progeny expressing said hybrid enzyme and said heterologous protein.

[0038] In one embodiment, the present disclosure contemplates a plant, comprising first and second expression vectors, said first vector comprising nucleic acid encoding a GNTIII enzyme, said second vector comprising nucleic acid encoding a heterologous protein. In another embodiment, the present disclosure contemplates the, wherein said heterologous protein is an antibody or antibody fragment.

BRIEF DESCRIPTION OF THE FIGURES

[0039]

Figures 1A and 1B show MALDI-TOF mass spectra of (A) N-linked glycans isolated from leaves of control tobacco plant and (B) N-linked glycans isolated from leaves of selected GnTM-17 tobacco plant transformed with human GnTIII. See, Table 1 for structures.

Figure 2 shows processing of high mannose type glycan (M9) to complex type glycans under the subsequent action of ManI, GnTI, ManII, and GnTII. It is also indicated what glycan structures the action of GalT and/or GNTIII at different points in chain of reactions would lead. The reactions catalyzed by fucosyltransferases and xylosyltransferases are not indicated. Core GlcNAc (Gn) is not indicated. Gn = GlcNAc; Gn^b = bisecting GlcNAc, G = galactose and M = mannose.

Figures 3A and 3B show (A) the T-DNA construct carrying the genes encoding glycan modifying enzymes to produce efficiently galactosylated bisected glycans that are devoid of immunogenic xylose and fucose and (B) the T-DNA construct carrying antibody light chain and heavy chain genes. TmXyl = transmembrane domain of xylosyltransferase, TmGnTI = transmembrane domain of GnT, P = promoter, R = selection marker, L = antibody light chain and H = antibody heavy chain.

Figures 4A and 4B show the nucleotide sequence (SEQ ID NO: 1, underlined portion of Figure 4(A) the protein sequence (SEQ ID NO: 2, underlined portion of Figure 4B) of *GnTIII* including a c-myc tag. Residues that can undergo conservative amino acid substitutions are defined in the DEFINITIONS section.

Figure 5A and 5B show a (A) map of the plasmid pDAB4005 and (B) the nucleotide sequence of the plasmid pDAB4005 (SEQ ID NO: 8).

Figure 6A and 6B show a (A) map of the plasmid pDAB7119 and (B) the nucleotide sequence of the plasmid pDAB7119 (SEQ ID NO: 9) including splice sites.

Figure 7A and 7B show a (A) map of the plasmid pDAB8504 and (B) the nucleotide sequence of the plasmid pDAB8504 (SEQ ID NO: 10).

Figure 8A and 8B show a (A) map of the plasmid pDAB7113 and (B) the nucleotide sequence of the plasmid pDAB7113 (SEQ ID NO: 11) including splice sites.

Figures 9A and 9B show MALDI-TOF mass spectra of glycoproteins from control and GnTIII corn. Comparison of mass spectra of N-glycans of glycoproteins isolated from calli of (A) control corn and of (B) selected GnTIII-corn. GnTIII corn was obtained through transformation with human GnTIII gene sequence and selection was performed by lectin blotting using E-PHA. See Table 3 for an annotation of the data contained in Figures 9A and 9B.

Figure 10 shows the full nucleotide sequence of *GnTIII* without a c-myc tag (SEQ ID NO: 7).

Figure 11 shows a MALDI-TOF mass spectra of glycoproteins from control and GnTIII corn-2. See, Table 4 for structures and abbreviations.

Figure 12 shows a representative blot of samples of transgenic maize callus for altered lectin binding due to expression of the *GnTIII* gene.

Figure 13 shows a representative blot of samples of transgenic maize callus for c-myc epitope expression.

Figures 14A and 14B show a MALDI-TOF mass spectra of glycoproteins from (A) control and (B) GnTIII corn plants.

DEFINITIONS

[0040] The terms "protein" and "polypeptide" refer to compounds comprising amino acids joined via peptide bonds and are used interchangeably. A "protein" or "polypeptide" encoded by a gene is not limited to the amino acid sequence

encoded by the gene, but includes post-translational modifications of the protein.

[0041] The term "glycoprotein" refers to proteins with covalently attached sugar units, either bonded via the OH group of serine or threonine (O glycosylated) or through the amide NH₂ of asparagine (N glycosylated). "Glycoprotein" may include, but is not limited to, for example, most secreted proteins (serum albumin is the major exception) and proteins exposed at the outer surface of the plasma membrane. Sugar residues found include, but are not limited to: mannose, N acetyl glucosamine, N acetyl galactosamine, galactose, fucose and sialic acid.

[0042] Where the term "amino acid sequence" is recited herein to refer to an amino acid sequence of a protein molecule, "amino acid sequence" and like terms, such as "polypeptide" or "protein" are not meant to limit the amino acid sequence to the complete, native amino acid sequence associated with the recited protein molecule. Furthermore, an "amino acid sequence" can be deduced from the nucleic acid sequence encoding the protein.

[0043] The term "portion" when used in reference to a protein (as in "a portion of a given protein") refers to fragments of that protein. The fragments may range in size from four amino acid residues to the entire amino sequence minus one amino acid.

[0044] The term "chimera" when used in reference to a polypeptide refers to the expression product of two or more coding sequences obtained from different genes, that have been cloned together and that, after translation, act as a single polypeptide sequence. Chimeric polypeptides are also referred to as "hybrid" polypeptides. The coding sequences includes those obtained from the same or from different species of organisms.

[0045] The term "fusion" when used in reference to a polypeptide refers to a chimeric protein containing a protein of interest joined to an exogenous protein fragment (the fusion partner). The fusion partner may serve various functions, including enhancement of solubility of the polypeptide of interest, as well as providing an "affinity tag" to allow purification of the recombinant fusion polypeptide from a host cell or from a supernatant or from both. If desired, the fusion partner may be removed from the protein of interest after or during purification.

[0046] The term "homolog" or "homologous" when used in reference to a polypeptide refers to a high degree of sequence identity between two polypeptides, or to a high degree of similarity between the three-dimensional structure or to a high degree of similarity between the active site and the mechanism of action. In a preferred embodiment, a homolog has a greater than 60 % sequence identity, and more preferably greater than 75% sequence identity, and still more preferably greater than 90 % sequence identity, with a reference sequence.

[0047] As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 90 percent sequence identity, more preferably at least 95 percent sequence identity or more (e.g., 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

[0048] The terms "variant" and "mutant" when used in reference to a polypeptide refer to an amino acid sequence that differs by one or more amino acids from another, usually related polypeptide. The variant may have "conservative" changes, wherein a substituted amino acid has similar structural or chemical properties. One type of conservative amino acid substitutions refers to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulfur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups are: valine (V) - leucine (L) -isoleucine (I), phenylalanine (F) -tyrosine (Y), lysine (K) -arginine (R), alanine (A) - valine (V), and asparagine (N) -glutamine (Q). More rarely, a variant may have "non-conservative" changes (e.g., replacement of a glycine with a tryptophan). Similar minor variations may also include amino acid deletions or insertions (i.e., additions), or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without abolishing biological activity may be found using computer programs well known in the art, for example, DNASTar software. Variants can be tested in functional assays. Preferred variants have less than 10 %, and preferably less than 5 %, and still more preferably less than 2 % changes (whether substitutions, deletions, and so on).

[0049] The term "domain" when used in reference to a polypeptide refers to a subsection of the polypeptide which possesses a unique structural and/or functional characteristic; typically, this characteristic is similar across diverse polypeptides. The subsection typically comprises contiguous amino acids, although it may also comprise amino acids which act in concert or which are in close proximity due to folding or other configurations.

[0050] The term "gene" refers to a nucleic acid (e.g., DNA or RNA) sequence that comprises coding sequences necessary for the production of an RNA, or a polypeptide or its precursor (e.g., proinsulin). A functional polypeptide can be encoded by a full length coding sequence or by any portion of the coding sequence as long as the desired activity or functional properties (e.g., enzymatic activity, ligand binding, signal transduction, etc.) of the polypeptide are retained. The term "portion" when used in reference to a gene refers to fragments of that gene. The fragments may range in size from a few nucleotides (e.g., ten nucleotides) to the entire gene sequence minus one nucleotide. Thus, "a nucleotide

comprising at least a portion of a gene" may comprise fragments of the gene or the entire gene.

[0051] The term "gene" also encompasses the coding regions of a structural gene and includes sequences located adjacent to the coding region on both the 5' and 3' ends for a distance of about 1 kb on either end such that the gene corresponds to the length of the full-length mRNA. The sequences which are located 5' of the coding region and which are present on the mRNA are referred to as 5' non-translated sequences. The sequences which are located 3' or downstream of the coding region and which are present on the mRNA are referred to as 3' non-translated sequences. The term "gene" encompasses both cDNA and genomic forms of a gene. A genomic form or clone of a gene contains the coding region interrupted with non-coding sequences termed "introns" or "intervening regions" or "intervening sequences." Introns are segments of a gene which are transcribed into nuclear RNA (hnRNA); introns may contain regulatory elements such as enhancers. Introns are removed or "spliced out" from the nuclear or primary transcript; introns therefore are absent in the messenger RNA (mRNA) transcript. The mRNA functions during translation to specify the sequence or order of amino acids in a nascent polypeptide.

[0052] In addition to containing introns, genomic forms of a gene may also include sequences located on both the 5' and 3' end of the sequences which are present on the RNA transcript. These sequences are referred to as "flanking" sequences or regions (these flanking sequences are located 5' or 3' to the non-translated sequences present on the mRNA transcript). The 5' flanking region may contain regulatory sequences such as promoters and enhancers which control or influence the transcription of the gene. The 3' flanking region may contain sequences which direct the termination of transcription, posttranscriptional cleavage and polyadenylation.

[0053] The term "heterologous" when used in reference to a gene refers to a gene encoding a factor that is not in its natural environment (*i.e.*, has been altered by the hand of man). For example, a heterologous gene includes a gene from one species introduced into another species. A heterologous gene also includes a gene native to an organism that has been altered in some way (*e.g.*, mutated, added in multiple copies, linked to a non-native promoter or enhancer sequence, *etc.*). Heterologous genes may comprise gene sequences that comprise cDNA forms of a gene; the cDNA sequences may be expressed in either a sense (to produce mRNA) or anti-sense orientation (to produce an anti-sense RNA transcript that is complementary to the mRNA transcript). Heterologous genes are distinguished from endogenous genes in that the heterologous gene sequences are typically joined to nucleotide sequences comprising regulatory elements such as promoters that are not found naturally associated with the gene for the protein encoded by the heterologous gene or with gene sequences in the chromosome, or are associated with portions of the chromosome not found in nature (*e.g.*, genes expressed in loci where the gene is not normally expressed).

[0054] A "heterologous glycoprotein" is a glycoprotein originating from a species other than the plant host system. The glycoprotein may include but is not limited to antibodies, hormones, growth factors, and growth factor receptors, antigens, cytokines and blood products.

[0055] A "plant host system" may include, but is not limited to, a plant or portion thereof which includes, but is not limited to, a plant cell, plant organ and/or plant tissue. The plant may be a monocotyledon (monocot) which is a flowering plant whose embryos have one cotyledon or seed leaf and includes but is not limited to lilies, grasses, corn (*Zea mays*), rice, grains including oats, wheat and barley, orchids, irises, onions and palms. Alternatively, the plant may be a dicotyledon (dicot) which includes, but is not limited to, tobacco (*Nicotiana*), tomatoes, potatoes, legumes (*e.g.*, alfalfa and soybeans), roses, daisies, cacti, violets and duckweed. The plant may also be a moss which includes, but is not limited to, *Physcomitrella patens*. The disclosure is further directed to a method for obtaining said bisected GlcNAc in a plant host system by introducing a nucleic acid encoding said GnTIII into a plant or portion thereof and expressing said GnTIII and isolating said plant or portion thereof expressing said GnTIII.

[0056] The term "nucleotide sequence of interest" or "nucleic acid sequence of interest" refers to any nucleotide sequence (*e.g.*, RNA or DNA), the manipulation of which may be deemed desirable for any reason (*e.g.*, treat disease, confer improved qualities, *etc.*), by one of ordinary skill in the art. Such nucleotide sequences include, but are not limited to, coding sequences of structural genes (*e.g.*, reporter genes, selection marker genes, oncogenes, drug resistance genes, growth factors, *etc.*), and non-coding regulatory sequences which do not encode an mRNA or protein product (*e.g.*, promoter sequence, polyadenylation sequence, termination sequence, enhancer sequence and other like sequences). The present disclosure contemplates host cells expressing a heterologous protein encoded by a nucleotide sequence of interest along with one or more hybrid enzymes.

[0057] The term "structural" when used in reference to a gene or to a nucleotide or nucleic acid sequence refers to a gene or a nucleotide or nucleic acid sequence whose ultimate expression product is a protein (such as an enzyme or a structural protein), an rRNA, an sRNA, a tRNA, *etc.*

[0058] The terms "oligonucleotide" or "polynucleotide" or "nucleotide" or "nucleic acid" refer to a molecule comprised of two or more deoxyribonucleotides or ribonucleotides, preferably more than three, and usually more than ten. The exact size will depend on many factors, which in turn depends on the ultimate function or use of the oligonucleotide. The oligonucleotide may be generated in any manner, including chemical synthesis, DNA replication, reverse transcription, or a combination thereof.

[0059] The terms "an oligonucleotide having a nucleotide sequence encoding a gene" or "a nucleic acid sequence

encoding" a specified polypeptide refer to a nucleic acid sequence comprising the coding region of a gene or in other words the nucleic acid sequence which encodes a gene product. The coding region may be present in either a cDNA, genomic DNA or RNA form. When present in a DNA form, the oligonucleotide may be single-stranded (*i.e.*, the sense strand) or double-stranded. Suitable control elements such as enhancers/promoters, splice junctions, polyadenylation signals, *etc.* may be placed in close proximity to the coding region of the gene if needed to permit proper initiation of transcription and/or correct processing of the primary RNA transcript. Alternatively, the coding region utilized in the expression vectors of the present invention may contain endogenous enhancers/promoters, splice junctions, intervening sequences, polyadenylation signals, *etc.* or a combination of both endogenous and exogenous control elements.

[0060] The term "recombinant" when made in reference to a nucleic acid molecule refers to a nucleic acid molecule which is comprised of segments of nucleic acid joined together by means of molecular biological techniques. The term "recombinant" when made in reference to a protein or a polypeptide refers to a protein molecule which is expressed using a recombinant nucleic acid molecule.

[0061] As used herein, the terms "complementary" or "complementarity" are used in reference to nucleotide sequences related by the base-pairing rules. For example, the sequence 5'-AGT-3' is complementary to the sequence 5'-ACT-3'. Complementarity can be "partial" or "total." "Partial" complementarity is where one or more nucleic acid bases is not matched according to the base pairing rules. "Total" or "complete" complementarity between nucleic acids is where each and every nucleic acid base is matched with another base under the base pairing rules. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands.

[0062] A "complement" of a nucleic acid sequence as used herein refers to a nucleotide sequence whose nucleic acids show total complementarity to the nucleic acids of the nucleic acid sequence. For example, the present disclosure contemplates the complements of SEQ ID NO: 1.

[0063] The term "homology" when used in relation to nucleic acids refers to a degree of complementarity. There may be partial homology (*i.e.*, partial identity) or complete homology (*i.e.*, complete identity). A partially complementary sequence is one that at least partially inhibits a completely complementary sequence from hybridizing to a target nucleic acid and is referred to using the functional term "substantially homologous." The inhibition of hybridization of the completely complementary sequence to the target sequence may be examined using a hybridization assay (Southern or Northern blot, solution hybridization and the like) under conditions of low stringency. A substantially homologous sequence or probe (*i.e.*, an oligonucleotide which is capable of hybridizing to another oligonucleotide of interest) will compete for and inhibit the binding (*i.e.*, the hybridization) of a completely homologous sequence to a target under conditions of low stringency. This is not to say that conditions of low stringency are such that non-specific binding is permitted; low stringency conditions require that the binding of two sequences to one another be a specific (*i.e.*, selective) interaction. The absence of non-specific binding may be tested by the use of a second target which lacks even a partial degree of complementarity (*e.g.*, less than about 30 % identity); in the absence of non-specific binding the probe will not hybridize to the second non-complementary target.

[0064] When used in reference to a double-stranded nucleic acid sequence such as a cDNA or genomic clone, the term "substantially homologous" refers to any probe which can hybridize to either or both strands of the double-stranded nucleic acid sequence under conditions of low stringency as described *infra*.

[0065] When used in reference to a single-stranded nucleic acid sequence, the term "substantially homologous" refers to any probe which can hybridize to the single-stranded nucleic acid sequence under conditions of low stringency as described *infra*.

[0066] The following terms are used to describe the sequence relationships between two or more polynucleotides: "reference sequence," "sequence identity," "percentage of sequence identity" and "substantial identity." A "reference sequence" is a defined sequence used as a basis for a sequence comparison; a reference sequence may be a subset of a larger sequence, for example, as a segment of a full-length cDNA sequence given in a sequence listing or may comprise a complete gene sequence. Generally, a reference sequence is at least 20 nucleotides in length, frequently at least 25 nucleotides in length, and often at least 50 nucleotides in length. Since two polynucleotides may each (1) comprise a sequence (*i.e.*, a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) may further comprise a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window," as used herein, refers to a conceptual segment of at least 20 contiguous nucleotide positions wherein a polynucleotide sequence may be compared to a reference sequence of at least 20 contiguous nucleotides and wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by the local homology algorithm of Smith and Waterman [Smith and Waterman, *Adv. Appl. Math.* 2: 482 (1981)] by the homology alignment algorithm of Needleman and Wunsch [Needleman and Wunsch, *J. Mol. Biol.* 48:443 (1970)], by the search

for similarity method of Pearson and Lipman [Pearson and Lipman, Proc. Natl. Acad. Sci. (U.S.A.) 85:2444 (1988)], by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, Wis.), or by inspection, and the best alignment (*i.e.*, resulting in the highest percentage of homology over the comparison window) generated by the various methods is selected. The term "sequence identity" means that two polynucleotide sequences are identical (*i.e.*, on a nucleotide-by-nucleotide basis) over the window of comparison. The term "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (*e.g.*, A, T, C, G, U, or I) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (*i.e.*, the window size), and multiplying the result by 100 to yield the percentage of sequence identity. The terms "substantial identity" as used herein denotes a characteristic of a polynucleotide sequence, wherein the polynucleotide comprises a sequence that has at least 85 percent sequence identity, preferably at least 90 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison window of at least 20 nucleotide positions, frequently over a window of at least 25-50 nucleotides, wherein the percentage of sequence identity is calculated by comparing the reference sequence to the polynucleotide sequence which may include deletions or additions which total 20 percent or less of the reference sequence over the window of comparison. The reference sequence may be a subset of a larger sequence, for example, as a segment of the full-length sequences of the compositions claimed in the present invention.

[0067] The term "hybridization" refers to the pairing of complementary nucleic acids. Hybridization and the strength of hybridization (*i.e.*, the strength of the association between the nucleic acids) is impacted by such factors as the degree of complementarity between the nucleic acids, stringency of the conditions involved, the T_m of the formed hybrid, and the G:C ratio within the nucleic acids. A single molecule that contains pairing of complementary nucleic acids within its structure is said to be "self hybridized."

[0068] The term " T_m " refers to the "melting temperature" of a nucleic acid. The melting temperature is the temperature at which a population of double-stranded nucleic acid molecules becomes half dissociated into single strands. The equation for calculating the T_m of nucleic acids is well known in the art. As indicated by standard references, a simple estimate of the T_m value may be calculated by the equation: $T_m = 81.5 + 0.41 (\% G + C)$, when a nucleic acid is in aqueous solution at 1 M NaCl (See *e.g.*, Anderson and Young, Quantitative Filter Hybridization, in Nucleic Acid Hybridization [1985]). Other references include more sophisticated computations that take structural as well as sequence characteristics into account for the calculation of T_m .

[0069] The term "stringency" refers to the conditions of temperature, ionic strength, and the presence of other compounds such as organic solvents, under which nucleic acid hybridizations are conducted. With "high stringency" conditions, nucleic acid base pairing will occur only between nucleic acid fragments that have a high frequency of complementary base sequences. Thus, conditions of "low" stringency are often required with nucleic acids that are derived from organisms that are genetically diverse, as the frequency of complementary sequences is usually less.

[0070] "Low stringency conditions" when used in reference to nucleic acid hybridization comprise conditions equivalent to binding or hybridization at 42 °C in a solution consisting of 5X SSPE (43.8 g/l NaCl, 6.9 g/l $\text{NaH}_2\text{PO}_4(\text{H}_2\text{O})$ and 1.85 g/l EDTA, pH adjusted to 7.4 with NaOH), 0.1% SDS, 5X Denhardt's reagent [50X Denhardt's contains per 500 ml: 5 g Ficoll (Type 400, Pharmacia), 5 g BSA (Fraction V; Sigma)] and 100 µg/ml denatured salmon sperm DNA followed by washing in a solution comprising 5X SSPE, 0.1% SDS at 42 °C when a probe of about 500 nucleotides in length is employed.

[0071] "Medium stringency conditions" when used in reference to nucleic acid hybridization comprise conditions equivalent to binding or hybridization at 42 °C in a solution consisting of 5X SSPE (43.8 g/l NaCl, 6.9 g/l $\text{NaH}_2\text{PO}_4(\text{H}_2\text{O})$ and 1.85 g/l EDTA, pH adjusted to 7.4 with NaOH), 0.5 % SDS, 5X Denhardt's reagent and 100 µg/ml denatured salmon sperm DNA followed by washing in a solution comprising 1.0X SSPE, 1.0 % SDS at 42 °C when a probe of about 500 nucleotides in length is employed.

[0072] "High stringency conditions" when used in reference to nucleic acid hybridization comprise conditions equivalent to binding or hybridization at 42 °C in a solution consisting of 5X SSPE (43.8 g/l NaCl, 6.9 g/l $\text{NaH}_2\text{PO}_4(\text{H}_2\text{O})$ and 1.85 g/l EDTA, pH adjusted to 7.4 with NaOH), 0.5 % SDS, 5X Denhardt's reagent and 100 µg/ml denatured salmon sperm DNA followed by washing in a solution comprising 0.1 X SSPE, 1.0 % SDS at 42 °C when a probe of about 500 nucleotides in length is employed.

[0073] It is well known that numerous equivalent conditions may be employed to comprise low stringency conditions; factors such as the length and nature (DNA, RNA, base composition) of the probe and nature of the target (DNA, RNA, base composition, present in solution or immobilized, etc.) and the concentration of the salts and other components (*e.g.*, the presence or absence of formamide, dextran sulfate, polyethylene glycol) are considered and the hybridization solution may be varied to generate conditions of low stringency hybridization different from, but equivalent to, the above listed conditions. In addition, the art knows conditions that promote hybridization under conditions of high stringency (*e.g.*, increasing the temperature of the hybridization and/or wash steps, the use of formamide in the hybridization

solution, etc.).

[0074] Additionally, the term "equivalent," when made in reference to a hybridization condition as it relates to a hybridization condition of interest, means that the hybridization condition and the hybridization condition of interest result in hybridization of nucleic acid sequences which have the same range of percent (%) homology. For example, if a hybridization condition of interest results in hybridization of a first nucleic acid sequence with other nucleic acid sequences that have from 50 % to 70 % homology to the first nucleic acid sequence, then another hybridization condition is said to be equivalent to the hybridization condition of interest if this other hybridization condition also results in hybridization of the first nucleic acid sequence with the other nucleic acid sequences that have from 50 % to 70 % homology to the first nucleic acid sequence.

[0075] When used in reference to nucleic acid hybridization the art knows well that numerous equivalent conditions may be employed to comprise either low or high stringency conditions; factors such as the length and nature (DNA, RNA, base composition) of the probe and nature of the target (DNA, RNA, base composition, present in solution or immobilized, etc.) and the concentration of the salts and other components (e.g., the presence or absence of formamide, dextran sulfate, polyethylene glycol) are considered and the hybridization solution may be varied to generate conditions of either low or high stringency hybridization different from, but equivalent to, the above-listed conditions.

[0076] The term "wild-type" when made in reference to a gene refers to a gene that has the characteristics of a gene isolated from a naturally occurring source. The term "wild-type" when made in reference to a gene product refers to a gene product that has the characteristics of a gene product isolated from a naturally occurring source. The term "naturally-occurring" as applied to an object refers to the fact that an object can be found in nature. For example, a polypeptide or polynucleotide sequence that is present in an organism (including viruses) that can be isolated from a source in nature and which has not been intentionally modified by man in the laboratory is naturally-occurring. A wild-type gene is frequently that gene which is most frequently observed in a population and is thus arbitrarily designated the "normal" or "wild-type" form of the gene. In contrast, the term "modified" or "mutant" when made in reference to a gene or to a gene product refers, respectively, to a gene or to a gene product which displays modifications in sequence and/or functional properties (i.e., altered characteristics) when compared to the wild-type gene or gene product. It is noted that naturally-occurring mutants can be isolated; these are identified by the fact that they have altered characteristics when compared to the wild-type gene or gene product.

[0077] Thus, the terms "variant" and "mutant" when used in reference to a nucleotide sequence refer to an nucleic acid sequence that differs by one or more nucleotides from another, usually related nucleotide acid sequence. A "variation" is a difference between two different nucleotide sequences; typically, one sequence is a reference sequence.

[0078] The term "polymorphic locus" refers to a genetic locus present in a population that shows variation between members of the population (i.e., the most common allele has a frequency of less than 0.95). Thus, "polymorphism" refers to the existence of a character in two or more variant forms in a population. A "single nucleotide polymorphism" (or SNP) refers a genetic locus of a single base which may be occupied by one of at least two different nucleotides. In contrast, a "monomorphic locus" refers to a genetic locus at which little or no variations are seen between members of the population (generally taken to be a locus at which the most common allele exceeds a frequency of 0.95 in the gene pool of the population).

[0079] A "frameshift mutation" refers to a mutation in a nucleotide sequence, usually resulting from insertion or deletion of a single nucleotide (or two or four nucleotides) which results in a change in the correct reading frame of a structural DNA sequence encoding a protein. The altered reading frame usually results in the translated amino-acid sequence being changed or truncated.

[0080] A "splice mutation" refers to any mutation that affects gene expression by affecting correct RNA splicing. Splicing mutation may be due to mutations at intron-exon boundaries which alter splice sites.

[0081] The term "detection assay" refers to an assay for detecting the presence or absence of a sequence or a variant nucleic acid sequence (e.g., mutation or polymorphism in a given allele of a particular gene, as e.g., *GnTIII* gene, SEQ ID NO: 1, Figure 4A), or for detecting the presence or absence of a particular protein (e.g., *GnTIII*, SEQ ID NO: 2, Figure 4B) or the structure or activity or effect of a particular protein (e.g., *GnTIII* activity), for detecting glycosylation moieties on a particular protein (e.g., N-linked glycans) or for detecting the presence or absence of a variant of a particular protein.

[0082] The term "antisense" refers to a deoxyribonucleotide sequence whose sequence of deoxyribonucleotide residues is in reverse 5' to 3' orientation in relation to the sequence of deoxyribonucleotide residues in a sense strand of a DNA duplex. A "sense strand" of a DNA duplex refers to a strand in a DNA duplex which is transcribed by a cell in its natural state into a "sense mRNA." Thus an "antisense" sequence is a sequence having the same sequence as the non-coding strand in a DNA duplex. The term "antisense RNA" refers to a RNA transcript that is complementary to all or part of a target primary transcript or mRNA and that blocks the expression of a target gene by interfering with the processing, transport and/or translation of its primary transcript or mRNA. The complementarity of an antisense RNA may be with any part of the specific gene transcript, i.e., at the 5' non-coding sequence, 3' non-coding sequence, introns, or the coding sequence. In addition, as used herein, antisense RNA may contain regions of ribozyme sequences that increase the efficacy of antisense RNA to block gene expression. "Ribozyme" refers to a catalytic RNA and includes sequence-

specific endoribonucleases. "Antisense inhibition" refers to the production of antisense RNA transcripts capable of preventing the expression of the target protein.

[0083] "Amplification" is a special case of nucleic acid replication involving template specificity. It is to be contrasted with non-specific template replication (*i.e.*, replication that is template-dependent but not dependent on a specific template). Template specificity is here distinguished from fidelity of replication (*i.e.*, synthesis of the proper polynucleotide sequence) and nucleotide (ribo- or deoxyribo-) specificity. Template specificity is frequently described in terms of "target" specificity. Target sequences are "targets" in the sense that they are sought to be sorted out from other nucleic acid. Amplification techniques have been designed primarily for this sorting out.

[0084] Template specificity is achieved in most amplification techniques by the choice of enzyme. Amplification enzymes are enzymes that, under conditions they are used, will process only specific sequences of nucleic acid in a heterogeneous mixture of nucleic acid. For example, in the case of Q β replicase, MDV-1 RNA is the specific template for the replicase (Kacian et al., Proc. Natl. Acad. Sci. USA, 69:3038, 1972). Other nucleic acid will not be replicated by this amplification enzyme. Similarly, in the case of T7 RNA polymerase, this amplification enzyme has a stringent specificity for its own promoters (Chamberlain et al., Nature, 228:227, 1970). In the case of T4 DNA ligase, the enzyme will not ligate the two oligonucleotides or polynucleotides, where there is a mismatch between the oligonucleotide or polynucleotide substrate and the template at the ligation junction (Wu and Wallace, Genomics, 4:560, 1989). Finally, *Taq* and *Pfu* polymerases, by virtue of their ability to function at high temperature, are found to display high specificity for the sequences bounded and thus defined by the primers; the high temperature results in thermodynamic conditions that favor primer hybridization with the target sequences and not hybridization with non-target sequences (H.A. Erlich (ed.), PCR Technology, Stockton Press, 1989).

[0085] The term "amplifiable nucleic acid" refers to nucleic acids that may be amplified by any amplification method. It is contemplated that "amplifiable nucleic acid" will usually comprise "sample template."

[0086] The term "sample template" refers to nucleic acid originating from a sample that is analyzed for the presence of "target" (defined below). In contrast, "background template" is used in reference to nucleic acid other than sample template that may or may not be present in a sample. Background template is most often inadvertent. It may be the result of carryover, or it may be due to the presence of nucleic acid contaminants sought to be purified away from the sample. For example, nucleic acids from organisms other than those to be detected may be present as background in a test sample.

[0087] The term "primer" refers to an oligonucleotide, whether occurring naturally as in a purified restriction digest or produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product which is complementary to a nucleic acid strand is induced, (*i.e.*, in the presence of nucleotides and an inducing agent such as DNA polymerase and at a suitable temperature and pH). The primer is preferably single stranded for maximum efficiency in amplification, but may alternatively be double stranded. If double stranded, the primer is first treated to separate its strands before being used to prepare extension products. Preferably, the primer is an oligodeoxyribonucleotide. The primer must be sufficiently long to prime the synthesis of extension products in the presence of the inducing agent. The exact lengths of the primers will depend on many factors, including temperature, source of primer and the use of the method.

[0088] The term "probe" refers to an oligonucleotide (*i.e.*, a sequence of nucleotides), whether occurring naturally as in a purified restriction digest or produced synthetically, recombinantly or by PCR amplification, that is capable of hybridizing to another oligonucleotide of interest. A probe may be single-stranded or double-stranded. Probes are useful in the detection, identification and isolation of particular gene sequences. It is contemplated that any probe used in the present invention will be labeled with any "reporter molecule," so that is detectable in any detection system, including, but not limited to enzyme (*e.g.*, ELISA, as well as enzyme-based histochemical assays), fluorescent, radioactive, and luminescent systems. It is not intended that the present disclosure be limited to any particular detection system or label.

[0089] The term "target," when used in reference to the polymerase chain reaction, refers to the region of nucleic acid bounded by the primers used for polymerase chain reaction. Thus, the "target" is sought to be sorted out from other nucleic acid sequences. A "segment" is defined as a region of nucleic acid within the target sequence.

[0090] The term "polymerase chain reaction" ("PCR") refers to the method of K.B. Mullis U.S. Patent Nos. 4,683,195, 4,683,202, and 4,965,188, that describe a method for increasing the concentration of a segment of a target sequence in a mixture of genomic DNA without cloning or purification. This process for amplifying the target sequence consists of introducing a large excess of two oligonucleotide primers to the DNA mixture containing the desired target sequence, followed by a precise sequence of thermal cycling in the presence of a DNA polymerase. The two primers are complementary to their respective strands of the double stranded target sequence. To effect amplification, the mixture is denatured and the primers then annealed to their complementary sequences within the target molecule. Following annealing, the primers are extended with a polymerase so as to form a new pair of complementary strands. The steps of denaturation, primer annealing, and polymerase extension can be repeated many times (*i.e.*, denaturation, annealing and extension constitute one "cycle"; there can be numerous "cycles") to obtain a high concentration of an amplified segment of the desired target sequence. The length of the amplified segment of the desired target sequence is determined by the relative

positions of the primers with respect to each other, and therefore, this length is a controllable parameter. By virtue of the repeating aspect of the process, the method is referred to as the "polymerase chain reaction" (hereinafter "PCR"). Because the desired amplified segments of the target sequence become the predominant sequences (in terms of concentration) in the mixture, they are said to be "PCR amplified."

5 [0091] With PCR, it is possible to amplify a single copy of a specific target sequence in genomic DNA to a level detectable by several different methodologies (e.g., hybridization with a labeled probe; incorporation of biotinylated primers followed by avidin-enzyme conjugate detection; incorporation of ³²P-labeled deoxynucleotide triphosphates, such as dCTP or dATP, into the amplified segment). In addition to genomic DNA, any oligonucleotide or polynucleotide sequence can be amplified with the appropriate set of primer molecules. In particular, the amplified segments created
10 by the PCR process itself are, themselves, efficient templates for subsequent PCR amplifications.

[0092] The terms "PCR product," "PCR fragment," and "amplification product" refer to the resultant mixture of compounds after two or more cycles of the PCR steps of denaturation, annealing and extension are complete. These terms encompass the case where there has been amplification of one or more segments of one or more target sequences.

15 [0093] The term "amplification reagents" refers to those reagents (deoxyribonucleotide triphosphates, buffer, etc.), needed for amplification except for primers, nucleic acid template, and the amplification enzyme. Typically, amplification reagents along with other reaction components are placed and contained in a reaction vessel (test tube, microwell, etc.).

[0094] The term "reverse-transcriptase" or "RT-PCR" refers to a type of PCR where the starting material is mRNA. The starting mRNA is enzymatically converted to complementary DNA or "cDNA" using a reverse transcriptase enzyme. The cDNA is then used as a "template" for a "PCR" reaction

20 [0095] The term "gene expression" refers to the process of converting genetic information encoded in a gene into RNA (e.g., mRNA, rRNA, tRNA, or snRNA) through "transcription" of the gene (i.e., via the enzymatic action of an RNA polymerase), and into protein, through "translation" of mRNA. Gene expression can be regulated at many stages in the process. "Up-regulation" or "activation" refers to regulation that increases the production of gene expression products (i.e., RNA or protein), while "down-regulation" or "repression" refers to regulation that decrease production. Molecules
25 (e.g., transcription factors) that are involved in up-regulation or down-regulation are often called "activators" and "repressors," respectively.

[0096] The terms "in operable combination," "in operable order" and "operably linked" refer to the linkage of nucleic acid sequences in such a manner that a nucleic acid molecule capable of directing the transcription of a given gene and/or the synthesis of a desired protein molecule is produced. The term also refers to the linkage of amino acid sequences
30 in such a manner so that a functional protein is produced.

[0097] The term "regulatory element" refers to a genetic element which controls some aspect of the expression of nucleic acid sequences. For example, a promoter is a regulatory element which facilitates the initiation of transcription of an operably linked coding region. Other regulatory elements are splicing signals, polyadenylation signals, termination signals, etc.

35 [0098] Transcriptional control signals in eukaryotes comprise "promoter" and "enhancer" elements. Promoters and enhancers consist of short arrays of DNA sequences that interact specifically with cellular proteins involved in transcription (Maniatis, et al., Science 236:1237, 1987). Promoter and enhancer elements have been isolated from a variety of eukaryotic sources including genes in yeast, insect, mammalian and plant cells. Promoter and enhancer elements have also been isolated from viruses and analogous control elements, such as promoters, are also found in prokaryotes. The
40 selection of a particular promoter and enhancer depends on the cell type used to express the protein of interest. Some eukaryotic promoters and enhancers have a broad host range while others are functional in a limited subset of cell types (for review, see Voss, et al., Trends Biochem. Sci., 11:287, 1986; and Maniatis, et al., supra 1987).

[0099] The terms "promoter element," "promoter" or "promoter sequence" refer to a DNA sequence that is located at the 5' end (i.e. precedes) of the coding region of a DNA polymer. The location of most promoters known in nature
45 precedes the transcribed region. The promoter functions as a switch, activating the expression of a gene. If the gene is activated, it is said to be transcribed, or participating in transcription. Transcription involves the synthesis of mRNA from the gene. The promoter, therefore, serves as a transcriptional regulatory element and also provides a site for initiation of transcription of the gene into mRNA.

50 [0100] Promoters may be tissue specific or cell specific. The term "tissue specific" as it applies to a promoter refers to a promoter that is capable of directing selective expression of a nucleotide sequence of interest to a specific type of tissue (e.g., petals) in the relative absence of expression of the same nucleotide sequence of interest in a different type of tissue (e.g., roots). Tissue specificity of a promoter may be evaluated by, for example, operably linking a reporter gene to the promoter sequence to generate a reporter construct, introducing the reporter construct into the genome of a plant such that the reporter construct is integrated into every tissue of the resulting transgenic plant, and detecting the
55 expression of the reporter gene (e.g., detecting mRNA, protein, or the activity of a protein encoded by the reporter gene) in different tissues of the transgenic plant. The detection of a greater level of expression of the reporter gene in one or more tissues relative to the level of expression of the reporter gene in other tissues shows that the promoter is specific for the tissues in which greater levels of expression are detected. The term "cell type specific" as applied to a promoter

refers to a promoter which is capable of directing selective expression of a nucleotide sequence of interest in a specific type of cell in the relative absence of expression of the same nucleotide sequence of interest in a different type of cell within the same tissue. The term "cell type specific" when applied to a promoter also means a promoter capable of promoting selective expression of a nucleotide sequence of interest in a region within a single tissue. Cell type specificity of a promoter may be assessed using methods well known in the art, e.g., immunohistochemical staining. Briefly, tissue sections are embedded in paraffin, and paraffin sections are reacted with a primary antibody which is specific for the polypeptide product encoded by the nucleotide sequence of interest whose expression is controlled by the promoter. A labeled (e.g., peroxidase conjugated) secondary antibody which is specific for the primary antibody is allowed to bind to the sectioned tissue and specific binding detected (e.g., with avidin/biotin) by microscopy.

[0101] Promoters may be constitutive or regulatable. The term "constitutive" when made in reference to a promoter means that the promoter is capable of directing transcription of an operably linked nucleic acid sequence in the absence of a stimulus (e.g., heat shock, chemicals, light, etc.). Typically, constitutive promoters are capable of directing expression of a transgene in substantially any cell and any tissue. In contrast, a "regulatable" promoter is one which is capable of directing a level of transcription of an operably linked nucleic acid sequence in the presence of a stimulus (e.g., heat shock, chemicals, light, etc.) which is different from the level of transcription of the operably linked nucleic acid sequence in the absence of the stimulus.

[0102] The terms "infecting" and "infection" with a bacterium refer to co-incubation of a target biological sample, (e.g., cell, tissue, etc.) with the bacterium under conditions such that nucleic acid sequences contained within the bacterium are introduced into one or more cells of the target biological sample.

[0103] The term "*Agrobacterium*" refers to a soil-borne, Gram-negative, rod-shaped phytopathogenic bacterium which causes crown gall. The term "*Agrobacterium*" includes, but is not limited to, the strains *Agrobacterium tumefaciens*, (which typically causes crown gall in infected plants), and *Agrobacterium rhizogens* (which causes hairy root disease in infected host plants). Infection of a plant cell with *Agrobacterium* generally results in the production of opines (e.g., nopaline, agropine, octopine etc.) by the infected cell. Thus, *Agrobacterium* strains which cause production of nopaline (e.g., strain LBA4301, C58, A208) are referred to as "nopaline-type" *Agrobacteria*; *Agrobacterium* strains which cause production of octopine (e.g., strain LBA4404, Ach5, B6) are referred to as "octopine-type" *Agrobacteria*; and *Agrobacterium* strains which cause production of agropine (e.g., strain EHA105, EHA101, A281) are referred to as "agropine-type" *Agrobacteria*.

[0104] The term "regulatory region" refers to a gene's 5' transcribed but untranslated regions, located immediately downstream from the promoter and ending just prior to the translational start of the gene.

[0105] The term "promoter region" refers to the region immediately upstream of the coding region of a DNA polymer, and is typically between about 500 bp and 4 kb in length, and is preferably about 1 to 1.5 kb in length.

[0106] In contrast, an "inducible" promoter is one which is capable of directing a level of transcription of an operably linked nucleic acid sequence in the presence of a stimulus (e.g., heat shock, chemicals, light, etc.) which is different from the level of transcription of the operably linked nucleic acid sequence in the absence of the stimulus.

[0107] The term "regulatory element" refers to a genetic element that controls some aspect of the expression of nucleic acid sequence(s). For example, a promoter is a regulatory element that facilitates the initiation of transcription of an operably linked coding region. Other regulatory elements are splicing signals, polyadenylation signals, termination signals, etc.

[0108] The enhancer and/or promoter may be "endogenous" or "exogenous" or "heterologous." An "endogenous" enhancer or promoter is one that is naturally linked with a given gene in the genome. An "exogenous" or "heterologous" enhancer or promoter is one that is placed in juxtaposition to a gene by means of genetic manipulation (i.e., molecular biological techniques) such that transcription of the gene is directed by the linked enhancer or promoter. For example, an endogenous promoter in operable combination with a first gene can be isolated, removed, and placed in operable combination with a second gene, thereby making it a "heterologous promoter" in operable combination with the second gene. A variety of such combinations are contemplated (e.g., the first and second genes can be from the same species, or from different species).

[0109] The term "naturally linked" or "naturally located" when used in reference to the relative positions of nucleic acid sequences means that the nucleic acid sequences exist in nature in the relative positions.

[0110] The presence of "splicing signals" on an expression vector often results in higher levels of expression of the recombinant transcript in eukaryotic host cells. Splicing signals mediate the removal of introns from the primary RNA transcript and consist of a splice donor and acceptor site (Sambrook, et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, New York [1989] pp. 16.7-16.8). A commonly used splice donor and acceptor site is the splice junction from the 16S RNA of SV40.

[0111] Efficient expression of recombinant DNA sequences in eukaryotic cells requires expression of signals directing the efficient termination and polyadenylation of the resulting transcript. Transcription termination signals are generally found downstream of the polyadenylation signal and are a few hundred nucleotides in length. The term "poly(A) site" or "poly(A) sequence" as used herein denotes a DNA sequence which directs both the termination and polyadenylation of

the nascent RNA transcript. Efficient polyadenylation of the recombinant transcript is desirable, as transcripts lacking a poly(A) tail are unstable and are rapidly degraded. The poly(A) signal utilized in an expression vector may be "heterologous" or "endogenous." An endogenous poly(A) signal is one that is found naturally at the 3' end of the coding region of a given gene in the genome. A heterologous poly(A) signal is one which has been isolated from one gene and positioned 3' to another gene. A commonly used heterologous poly(A) signal is the SV40 poly(A) signal. The SV40 poly(A) signal is contained on a 237 bp *Bam*HII/*Bcl*I restriction fragment and directs both termination and polyadenylation (Sambrook, *supra*, at 16.6-16.7).

[0112] The term "vector" refers to any genetic element, such as a plasmid, phage, transposon, cosmid, chromosome, retrovirus, virion, or similar genetic element, which is capable of replication when associated with the proper control elements and which can transfer gene sequences into cells and/or between cells. Thus, this term includes cloning and expression vehicles, as well as viral vectors.

[0113] The term "expression vector" as used herein refers to a recombinant DNA molecule containing a desired coding sequence (or coding sequences) - such as the coding sequence(s) for the hybrid enzyme(s) described in more detail below - and appropriate nucleic acid sequences necessary for the expression of the operably linked coding sequence in a particular host cell or organism. Nucleic acid sequences necessary for expression in prokaryotes usually include a promoter, an operator (optional), and a ribosome binding site, often along with other sequences. Eukaryotic cells are known to utilize promoters, enhancers, and termination and polyadenylation signals. It is not intended that the present disclosure be limited to particular expression vectors or expression vectors with particular elements.

[0114] The term "transfection" refers to the introduction of foreign DNA into cells. Transfection may be accomplished by a variety of means known to the art including calcium phosphate-DNA co-precipitation, DEAE-dextran-mediated transfection, polybrene-mediated transfection, glass beads, electroporation, microinjection, liposome fusion, lipofection, protoplast fusion, viral infection, biolistics (*i.e.*, particle bombardment) and the like.

[0115] The term "stable transfection" or "stably transfected" refers to the introduction and integration of foreign DNA into the genome of the transfected cell. The term "stable transfectant" refers to a cell that has stably integrated foreign DNA into the genomic DNA.

[0116] The term "transient transfection" or "transiently transfected" refers to the introduction of foreign DNA into a cell where the foreign DNA fails to integrate into the genome of the transfected cell. The foreign DNA persists in the nucleus of the transfected cell for several days. During this time the foreign DNA is subject to the regulatory controls that govern the expression of endogenous genes in the chromosomes. The term "transient transfectant" refers to cells that have taken up foreign DNA but have failed to integrate this DNA.

[0117] The term "calcium phosphate co-precipitation" refers to a technique for the introduction of nucleic acids into a cell. The uptake of nucleic acids by cells is enhanced when the nucleic acid is presented as a calcium phosphate-nucleic acid co-precipitate. The original technique of Graham and van der Eb (Graham and van der Eb, *Virology*, 52:456, 1973), has been modified by several groups to optimize conditions for particular types of cells. The art is well aware of these numerous modifications.

[0118] The terms "bombarding," "bombardment," and "biolistic bombardment" refer to the process of accelerating particles towards a target biological sample (*e.g.*, cell, tissue, *etc.*) to effect wounding of the cell membrane of a cell in the target biological sample and/or entry of the particles into the target biological sample. Methods for biolistic bombardment are known in the art (*e.g.*, U.S. Patent No. 5,584,807), and are commercially available (*e.g.*, the helium gas-driven microprojectile accelerator (PDS-1000/He, BioRad).

[0119] The term "microwounding" when made in reference to plant tissue refers to the introduction of microscopic wounds in that tissue. Microwounding may be achieved by, for example, particle bombardment as described herein.

[0120] The term "plant" as used herein refers to a plurality of plant cells which are largely differentiated into a structure that is present at any stage of a plant's development. Such structures include, but are not limited to, a fruit, shoot, stem, leaf, flower petal, *etc.* The term "plant tissue" includes differentiated and undifferentiated tissues of plants including, but not limited to, roots, shoots, leaves, pollen, seeds, tumor tissue and various types of cells in culture (*e.g.*, single cells, protoplasts, embryos, callus, protocorm-like bodies, *etc.*). Plant tissue may be *in planta*, in organ culture, tissue culture, or cell culture. Similarly, "plant cell(s)" may be cells in culture or may be part of a plant.

[0121] The term "transgenic" when used in reference to a cell refers to a cell which contains a transgene, or whose genome has been altered by the introduction of a transgene. The term "transgenic" when used in reference to a cell, tissue or to a plant refers to a cell, tissue or plant, respectively, which comprises a transgene, where one or more cells of the tissue contain a transgene (such as a gene encoding the hybrid enzyme(s) disclosed herein), or a plant whose genome has been altered by the introduction of a transgene. Transgenic cells, tissues and plants may be produced by several methods including the introduction of a "transgene" comprising nucleic acid (usually DNA) into a target cell or integration of the transgene into a chromosome of a target cell by way of human intervention, such as by the methods described herein.

[0122] The term "transgene" as used herein refers to any nucleic acid sequence which is introduced into the genome of a cell by experimental manipulations. A transgene may be an "endogenous DNA sequence," or a "heterologous DNA