

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN

Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS

Prior Appl. No.: 15/292,731

Prior Appl. Filing
Date: 10/13/2016

Examiner: Unassigned

Art Unit: Unassigned

CONTINUING PATENT APPLICATION
TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Transmitted herewith for filing under 37 C.F.R. § 1.53(b) is a:

☐ Continuation ☒ Division ☐ Continuation-In-Part (CIP)

of the above-identified copending prior application in which no patenting, abandonment, or termination of proceedings has occurred. Priority to the above-identified prior application is hereby claimed under 35 U.S.C. § 120 for this continuing application. The entire disclosure of the above-identified prior application is considered as being part of the disclosure of the accompanying continuing application and is hereby incorporated by reference therein.

Enclosed are:

☒ Description, Claim(s), and Abstract (18 pages).

☒ Formal drawings (7 sheets, Figures 1-8).

☒ Executed Declaration (3 pages).

- [X] Power of Attorney (2 pages).
- [X] Information Disclosure Statement.
- [X] Form PTO-SB08 (3 pages).
- [X] Application Data Sheet (37 CFR 1.76).

The adjustment to the number of sheets for EFS-Web filing follows:

Number of Sheets		EFS-Web Adjustment	Number of Sheets for EFS-Web
24	x	75%	18

The filing fee is calculated below at the large entity rate:

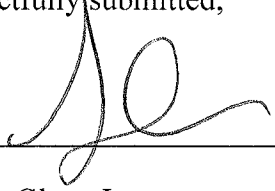
	Number Filed	Included in Basic Fee	Extra		Rate		Fee Totals
Basic Filing Fee					\$300.00	=	\$300.00
Search Fee					\$660.00		\$660.00
Examination Fee					\$760.00		\$760.00
Sequence Listing fee							\$0.00
Size Fee	18	- 100	= 0	x	\$400.00		\$0.00
Total	15	- 20	= 0	x	\$100.00	=	\$0.00
Claims:							
Independents	1	- 3	= 0	x	\$460.00	=	\$0.00
:							
If any Multiple Dependent Claim(s) present:				+	\$820.00	=	\$0.00
Surcharge under 37 CFR 1.16(e) for late filing of Executed Declaration or late payment of filing fee				+	\$160.00	=	\$0.00
Prioritized Examination fee (Track I) under 37 C.F.R. § 1.17 (c)							\$0.00
Processing Fee (Track I) under 37 C.F.R. § 1.17 (i)							\$0.00
TOTAL FILING FEE:						=	\$1720.00
Assignment Recordation Fee:				+	\$50.00	=	\$0.00
Processing Fee under 37 CFR 1.17(i) for Late Filing of English Translation of Application:				+	\$140.00	=	\$0.00
TOTAL FEE						=	\$1720.00

The above-identified fees of \$1720.00 are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any fees required to secure a filing date and maintain pendency of this application to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 14, 2020

By 

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 Remove				
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
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Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
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Inventor 2 Remove				
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
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Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
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Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410	
		Application Number		
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS			

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All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.					

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).			
☐ An Address is being provided for the correspondence Information of this application.			
Customer Number	22428		
Email Address	IPDocketing@foley.com	<input type="button" value="Add Email"/>	<input type="button" value="Remove Email"/>

Application Information:

Title of the Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		
Attorney Docket Number	067286-0410	Small Entity Status Claimed	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	7	Suggested Figure for Publication (if any)	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)
☐ Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application has not and will not be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	☒ Customer Number	☐ US Patent Practitioner	☐ Limited Recognition (37 CFR 11.9)
Customer Number	22428		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Division of	15/292731	2016-10-13
Prior Application Status		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15/292731	Claims benefit of provisional	62/241902	2015-10-15
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button.			

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)¹ the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

			Remove
Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ^j (if applicable)
Additional Foreign Priority Data may be generated within this form by selecting the Add button.			

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

<p>This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.</p> <p>☐ NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.</p>
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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

[Clear](#)

☒ Assignee
 ☐ Legal Representative under 35 U.S.C. 117
 ☐ Joint Inventor

☐ Person to whom the inventor is obligated to assign.
 ☐ Person who shows sufficient proprietary interest

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name DUSA Pharmaceuticals, Inc.

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Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button.

Assignee Information including Non-Applicant Assignee Information:

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

If the Assignee or Non-Applicant Assignee is an Organization check here. ☒

Organization Name

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MA

Countryⁱ

Postal Code

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Phone Number

Fax Number

Email Address

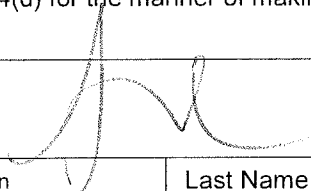
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the **INITIAL** filing of the application and either box A or B is **not** checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature			Date (YYYY-MM-DD)	2020-02-14	
First Name	Glenn	Last Name	Law	Registration Number	34371
Additional Signature may be generated within this form by selecting the Add button.					

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	067286-0410
		Application Number	
Title of Invention	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS		

This collection of information is required by 37 CFR 1.76. 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 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet 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.**

ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a divisional application of U.S. Application serial number 15/292,731, filed October 13, 2016, which claims the benefit of priority to U.S. Provisional Application No. 62/241,902 filed on October 15, 2015, the entire contents of all of which are incorporated herein by reference.

FIELD

[0002] The invention relates generally to an adjustable illuminator that provides a uniform distribution of visible light in a number of configurations and is suitable for use in photodynamic therapy and diagnosis.

BACKGROUND

[0003] Photodynamic therapy (PDT), photodynamic diagnosis (PD), or photochemotherapy is generally used to treat and/or diagnose several types of ailments in or near the skin or other tissues, such as those in a body cavity. For example, PDT or PD may be used for treatment or diagnosis of actinic keratosis of the scalp or facial areas of a patient. In addition, PDT and PD may be used for treatment and diagnosis of other indications (e.g., acne, warts, psoriasis, photo-damaged skin, cancer) and other areas of the patient (e.g., arms, legs).

[0004] During one form of PDT or PD, a patient is first administered a photoactivatable agent or a precursor of a photoactivatable agent that accumulates in the tissue to be treated or diagnosed. The area in which the photoactivatable agent is administered is then exposed to visible light, which causes chemical and/or biological changes in the agent. These changes allow the agent to then selectively locate, destroy, or alter the target tissue while, at the same time, causing only mild and reversible damage to other tissues in the treatment area. One example of a precursor of a photoactivatable agent is 5-aminolevulinic acid ("ALA"), which is commonly used in PDT of actinic keratosis. As they are used here, the terms ALA or 5-aminolevulinic acid refer to ALA itself, precursors thereof and pharmaceutically acceptable salts of the same.

[0005] For effective treatment, it is desirable to have a power output that is uniform in intensity and color. Illuminators, such as those disclosed in U.S. Patent Nos. 8,758,418; 8,216,289; 8,030,836; 7,723,910; 7,190,109; 6,709,446; 6,223,071, which are incorporated by reference in their entireties for the techniques, methods, compositions, and devices related to PDT and PD, are typically used to provide the proper uniformity of light for treatment purposes. These devices generally include a light source (e.g., a fluorescent tube), coupling elements that direct, filter or otherwise conduct emitted light so that it arrives at its intended target in a usable form, and a control system that starts and stops the production of light when necessary.

SUMMARY

[0006] Because PDT can be used to treat a variety of treatment areas, some illuminators utilize two or more panels, each panel having a light source to emit light at the intended target area. These panels are coupled together so as to be rotatable relative to each other. By incorporating multiple, rotatable panels, the overall size and shape of the area that is illuminated can be changed according to the intended treatment area.

[0007] In conventional adjustable illuminators, the panels are equally sized by width and length and are typically driven at the same power level. The panels are further joined at their edges by hinges so as to be rotatable to achieve a desired configuration. However, due to the edges of the panels and the presence of the hinges, the light source(s) of one panel does not immediately adjoin the light source(s) of an adjacent panel. As a result, light is not emitted from a “gap” between the light sources. The lack of light emitting from such areas, together with the uniform supply of power to the panels, can cause optical “dead space” in certain portions of the target treatment area. These portions, in turn, receive less overall light, resulting in a lower dose of treatment in those portions. In some instances, the dose of treatment can be lowered by as much as a factor of five when compared with those areas receiving an optimal amount of light.

[0008] Generally, these conventional illuminators are used for phototherapy of acne, which typically does not require the administration of a photoactivatable agent for effective treatment. Thus, exposure to the light alone is generally sufficient treatment. Moreover, because multiple treatment sessions can be utilized to effectively treat the condition, uniformity of light across the target area during a given treatment is less of a concern in some situations. However, some

forms of treatment involving PDT, such as the use of ALA to treat actinic keratosis, require specific and highly uniform intensity and color of light to achieve effectiveness. In these instances, successful PDT relies on the targeted delivery of both the correct quantity of the photoactivatable agent and the correct quantity (i.e., power and wavelength) of light to produce the desired photochemical reactions in the target cells. Thus, to achieve this, the light source must provide illumination to the target area and this illumination must be uniform with respect to both wavelength and power. The optical dead space that can occur at or near the hinges of conventional adjustable illuminators reduces the uniformity of the light along the treatment area, thereby reducing the effectiveness of PDT for these specific treatments. Moreover, these illuminators are also configured to adjust within a limited range, such that only a limited amount of surfaces on a patient's body may be treated, such as a patient's face and scalp. In addition, due to the various contours of a patient's body, the uniformity of light delivered by these conventional illuminators may vary substantially depending on the treatment area of the patient.

[0009] Therefore, it is an object of some embodiments of the present invention to reduce or eliminate these dead spaces and provide for a more uniform light distribution in an adjustable illuminator designed for PDT or PD of a variety of targeted areas. In addition, it is an object of some embodiments of the present invention to provide an infinitely adjustable illuminator that can effectively deliver a uniformity of light across various areas of a patient's body, such as a patient's extremities (e.g., arms and legs) or torso, in addition to a patient's face and scalp. Thus, a uniform light may be delivered to a targeted treatment area regardless of the shape and location of the contoured surface of the patient's body.

[0010] One embodiment of the present invention uses a plurality of panels, wherein at least one panel is of a different width than the other panels. This panel is positioned between two other panels and, in a way, acts as a "lighted hinge" to provide enough "fill-in" light to reduce or eliminate the optical dead spaces when the panels are bent into a certain configuration. Preferably, five panels in total are used to provide for an optimal increase in the total size of possible treatment areas. Two of the panels are preferably of a smaller width than the other three larger panels. These panels are positioned in an alternating manner such that each of the smaller-width panels is situated in between two of the three larger panels to allow for both adjustability and increased uniformity. Furthermore, to further reduce or eliminate optical dead spaces, the

panels are preferably coupled together using nested hinges, thereby reducing the area in which no light source is present on the illuminator. In order to even further reduce or eliminate optical dead spaces, it is preferable that the light sources on each of the panels are individually configurable to provide specific power output to certain areas of the light sources on the panels to compensate for decreased uniformity. For example, the power outputted to each individual diode in an array of light emitting diodes (LED) may be individually adjusted.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] Features, aspects, and advantages of the present invention will become apparent from the following description and the accompanying exemplary embodiments shown in the drawings, which are briefly described below.

[0012] FIGS. 1A-1B show top views of a main body of an illuminator according to an exemplary embodiment.

[0013] FIGS. 2A-2B show perspective views of the main body of the illuminator of FIGS. 1A-1B.

[0014] FIGS. 3A-3B show detailed views of the nested hinges of the main body of the illuminator of FIGS. 1A-1B.

[0015] FIG. 4 shows a perspective view of the illuminator having the main body of FIGS. 1A-1B mounted to a stand.

[0016] FIG. 5 shows a schematic view illustrating an addressable configuration of LEDs mounted on the main body of the illuminator of FIGS. 1A-1B.

[0017] FIG. 6 shows a schematic view illustrating widths and lengths of individual panels of the main body of the illuminator of FIGS. 1A-1B.

[0018] FIG. 7 shows a graph illustrating light dosage across a treatment area according to a conventional paneled illuminator.

[0019] FIG. 8 shows a graph illustrating light dosage across the same treatment area as FIG. 7 using an illuminator according to one embodiment of the present invention.

DETAILED DESCRIPTION

[0020] FIGS. 1A-1B and 2A-2B illustrate one embodiment of a configurable illuminator according to the present invention. The illuminator includes a main body 100, which preferably has five individual panels 10a-10e, each of which are connected in a rotatable manner via nested hinges 50. Each panel contains an array of light emitting diodes (LED) 60, which may be configured in an evenly spaced pattern across the face of the panel. The number of individual LEDs arranged in a given array is not particularly limited. Alternatively, other types of light sources may be used, such as fluorescent or halogen lamps.

[0021] Preferably, each LED array 60 extends as far to the edges as possible. In addition, the LED arrays 60 are preferably dimensioned to provide an overall lighted area for a given treatment area based on a range from the 5th percentile of corresponding female sizes to the 95th percentile of corresponding male sizes for that particular treatment area. The LED arrays 60 emit light at an appropriate wavelength according to the intended treatment or to activate the particular photoactivatable agent used in treatment or diagnosis. For example, when ALA is used as a precursor of a photoactivatable agent for the treatment of actinic keratosis, the LED arrays 60 preferably emit blue light having wavelengths at or above 400 nanometers (nm), for example, about 430 nm, about 420 nm or, for example, 417 nm. However, the LED arrays 60 may also emit visible light in other ranges of the spectrum, such as in the green and/or red ranges between 400 and 700 nm, for example, about 625 nm to 640 nm or, for example, 635 nm. For example, the LED arrays 60 may also emit light having wavelengths of 510 nm, 540 nm, 575 nm, 630 nm, or 635 nm. In addition, the LED arrays 60 may be configured to emit light continuously or the LED arrays 60 may be configured to flash the diodes on and off based on a predetermined interval. Furthermore, the LED arrays 60 may be configured such that only one wavelength of light (e.g., blue) is emitted. Alternatively, the LED arrays 60 may be configured such that two or more wavelengths of light are emitted from the arrays. For example, the LED arrays 60 may be configured to alternately emit blue light and red light for treatment purposes.

[0022] As shown in FIGS. 1A-1B and 2A-2B, the five panels 10a-10e are of different widths relative to one another. In particular, in certain embodiments, three panels 10a, 10c, 10e are configured to have wider widths, while two panels 10b, 10d have smaller, narrower widths, each of the narrower widths of the two panels 10b, 10d being less than each of the wider widths of the three panels 10a, 10c, 10e. In some embodiments, the wider widths of the three larger panels 10a, 10c, 10e are approximately equal. In other embodiments, the wider widths of the three larger panels 10a, 10c, 10e are different relative to one another. In addition, the narrower widths of the two panels 10b, 10d may be approximately equal or may be different relative to one another. The panels are further arranged in an alternating configuration, with the narrower panels (e.g., 10b) positioned in between two wider panels (e.g., 10a, 10c). As shown in FIG. 6, in some embodiments, the narrower panels 10b, 10d are configured to have a width that is about 30% to 60% less than the width of the wider panels 10a, 10c, 10e. In other embodiments, the narrower panels 10b, 10d are configured to have a width that is about 30% to 50% less than the width of the wider panels 10a, 10c, 10e.

[0023] As shown in FIGS. 1A-1B and 2A-2B, the panels 10a-10e are rotatably connected by hinges 50. The hinges 50 may take the form of nested hinges, which may include hinges that substantially reduce or eliminate optical dead spaces. As shown in FIGS. 2A-2B, on at least one side of a panel, a tab 23 may extend out from both the top and bottom of the panel. The tabs 23 are configured such that a side of an adjacent panel may be received between the tabs 23, as shown in FIG. 2A. Thus, as best seen in FIGS. 2A-2B and 6, the height of the adjacent panel (e.g., panel 10a) is slightly smaller than the height of the tabbed panel (e.g., panel 10b) into which the adjacent panel is received. As shown in FIG. 6, the middle panel (i.e., panel 10c) is preferably configured as having the largest height, such that it is tabbed on both sides and may receive the sides of adjacent panels on each side. As seen in FIGS. 1A-1B, each of the tabs 23 further includes an opening to receive a bolt to connect adjacent panels together.

[0024] As shown in further detail in FIGS. 3A-3B, between the tabs 23 are the nested hinges 50, which are mounted to the inner side surfaces of adjacent panels (e.g., 10a, 10b) to allow for rotation of the panels. A flange 51 of the hinge 50 is mounted to the inner side surface of a panel via bolts 53. The inner side surface of a panel may include a recess in which the flange 51 may be placed. The inner side surface of the panel may also include an additional recess to

accommodate the joint of the hinge 50 such that the joint of the hinge 50 becomes substantially flush with an outer front surface of the panel. Such configurations may allow for the outside vertical edges of adjoining panels to be positioned closer to one another. By spacing the vertical edges of adjoining panels closer, optical dead spaces may be further reduced or eliminated. In addition, the hinges 50 together with the tabs 23 may reduce the number of pinch points present in the system.

[0025] As shown in FIGS. 1A-1B, the main body 100 of the illuminator may include a mounting head 40. The mounting head 40 may allow for the main body 100 to be mounted to a movable stand 80, which is shown in FIG. 4, to allow a user to easily move the main body 100 to the appropriate treatment position. The stand 80 includes a base 81 and a vertical pillar 82. The base 81 may further include wheels 87 at its bottom in order to allow the user to horizontally move the illuminator to an appropriate position. The wheels 87 may include locks, such that the stand 80 is prevented from further horizontal movement once positioned. In addition, the vertical pillar 82 may be attached to the base 81 at a pivot point 83. The pivot point 83 allows the vertical pillar 82 to be rotated to increase the range of positioning for the illuminator. At a top end, the vertical pillar 82 includes a connecting arm 85, which may serve as a mounting structure for the main body 100. The connecting arm 85 includes a hinge point 86 such that the main body 100 can be moved vertically relative to the stand 80. The vertical pillar 82 may also be configured as a telescopic structure, such that the user can change the height of the vertical pillar 82. This allows for an increased range of vertical movement for the main body 100, which can allow the user to position the main body 100 at lower portions of a treatment area, such as a patient's legs or feet. The stand 80 may also include a stabilization arm 84. Once the stand 80 and main body 100 is positioned, the stabilization arm 84 may be attached to the main body 100 to prevent unwanted movement of the main body 100 during treatment. As further shown in FIG. 4, a controller and power supply 90 is mounted to the stand 80 in order to supply electrical power to the main body 100 and allow the user to control the main body 100 for treatment purposes. Alternatively, the controller and power supply 90 may be directly mounted to the main body 100. In order to provide a cooling system for the LED arrays 60, one or more fans 70 may be mounted onto each of the panels, as shown in FIG. 4.

[0026] At least one control unit is also connected to the panels to regulate power to the lights to achieve the required uniformity and intensity for the target treatment. The control unit may be implemented as hardware, software, or a combination of both, such as a memory device storing a computer program and a processor to execute the program. Alternatively, each panel may have a dedicated control unit to regulate power to the individual LED array on a given panel to allow for more particular fine-tuning of the illuminator, which may further enhance uniformity and increase efficiency. For example, under Lambert's cosine law, light intensity at a given point on a "Lambertian" surface (such as skin) is directly proportional to the cosine of the angle between the incoming ray of light and the normal to the surface. Thus, a ray of light that is directed to the front of a curved surface (e.g., a head of a patient) will arrive in a substantially perpendicular manner to that area and will result in 100% absorbance. However, a ray of light that arrives at a side edge of the curved surface will arrive in a substantially parallel manner. According to Lambert's cosine law, the intensity, and thus absorption, of the light at the side edge will approach zero, making treatment at that area ineffective. Thus, a "fall off" of light exposure tends to occur at the edges of a curved surface. In addition, "fall off" increases as the distance between the light source and the point on the surface increases.

[0027] Configuring an illuminator to conform to the curved surface (e.g., a U-shaped configuration designed to "wrap around" the curvature of the surface) aids in reducing this effect and increases overall uniformity. However, to sufficiently increase uniformity, the light source should be larger relative to the target treatment area in order to fully encompass the body part to be treated and also provide light from all angles to any target point on the treatment area. In order to increase the uniformity of light exposure to the treatment area while maintaining a practical size of the illuminator, the LED arrays 60 may be individually configured to increase the intensity of light emitting from certain diodes to compensate for this fall-off effect.

[0028] An example in which the LED arrays 60 may be individually configured is shown in FIG. 5. Here, the LED arrays 60 are divided into three general areas, which may be described as "addressable strings." Areas 1, 3, and 5 correspond to an addressable string configuration that may be included in the wider panels 10a, 10c, and 10e, while areas 2, 4, and 6 correspond to an addressable string configuration that may be included in the narrower panels 10b and 10d. The current to each area is adjusted in order to adjust the intensity of light emitting from each of the

areas. For example, a higher current may be supplied to areas 1 and 2 than the current supplied to areas 3 and 4 such that areas 1 and 2 emit a higher intensity of light than areas 3 and 4. Similarly, a higher current may be supplied to areas 3 and 4 than the current supplied to areas 5 and 6. Thus, a higher intensity of light is emitted overall from the edges, which may allow for a reduction in any fall-off effect. Alternatively, the illuminator may be configured to adjust each individual diode present in a given LED array 60, allowing for an even greater fine-tuning effect. Furthermore, by using either pre-programmed settings or sensors to detect the curvature of the surface to be treated, the LED arrays 60 can be individually configured to emit more intense light to only those areas that require it. This allows for an increase in uniformity of light exposure in an efficient manner as power output and/or light intensity is increased to only certain diodes, in accordance with need.

[0029] The addressable strings of the LED arrays 60 may also include varying amounts of individual diodes mounted within the particular area. For example, for the wider panels 10a, 10c, and 10e, 12 diodes may be mounted in each of areas 1, while 9 diodes may be mounted in each of areas 3 and 41 diodes may be mounted in area 5, resulting in a total of 83 individual diodes included within each of the wider panels 10a, 10c, and 10e. For the narrower panels 10b and 10d, 8 diodes may be mounted in each of areas 2, while 9 diodes may be mounted in each of areas 4, and 23 diodes may be mounted in area 6, resulting in a total of 57 individual diodes included within each of the narrower panels 10b and 10d. However, the number and arrangement of diodes included within each of the LED arrays 60 is not particularly limited. For example, the wider panels 10a, 10c, and 10e may each contain a total amount of diodes that ranges from about 80 diodes to about 350 diodes. Similarly, the narrower panels 10b and 10d may each contain a total amount of diodes that ranges from about 50 diodes to about 250 diodes. By varying the arrangement of the diodes within each of the addressable strings of the LED arrays 60, power output and/or the intensity of light emitted from a given array may be better controlled and fine-tuned.

[0030] In addition, individually regulating power to the LED arrays 60 can also contribute to the reduction or elimination of the optical dead spaces that may otherwise occur at the hinge points. Specifically, power output and/or the emitted light intensity may be increased close to the edges of the array that are closest to the nested hinges to compensate for the lack of light

emitting from the meeting point of panels. The narrower panels 10b, 10d are also preferably operated at a higher power level and/or at a higher emitted light intensity compared to the wider panels 10a, 10c, 10e in order to provide additional fill-in light. Furthermore, individual power regulation may aid in compensating for manufacturing variance that can occur in individual diodes. Finally, by fine-tuning each array 60, the panels can be easily deployed for other applications as each array is specifically configurable to address the lighting needs of the specific application.

[0031] The illuminator may further include a timer, which can indicate to the user the appropriate length of exposure time for the particular treatment. The illuminator may also be programmed with pre-stored light dosing parameters to allow the user to select a desired treatment type. The pre-stored parameters may include, for example, pre-stored settings for exposure time, light intensity, and outputted wavelength. Based on the selected treatment, the illuminator is automatically configured to provide the correct lighting dosage by being supplied with the appropriate power output to achieve the required uniformity for the treatment. Alternatively, the illuminator can be provided with sensors that detect the size of the treatment area positioned in front of the illuminator. The sensors then determine the correct light dosing parameters based on the sensed treatment area. The illuminator may also further include actuators and may be programmed to be moved automatically depending on the selected treatment. Once a treatment is selected, the illuminator may be automatically positioned into the proper configuration by the actuators without requiring the user to move the system by hand. Alternatively, the sensors may detect the adjusted position of the illuminator manually set by the user. The detected position of the illuminator may then be used to indicate the intended treatment area. Correct light dosing parameters for the specific treatment area may then be provided based on the detected position set by the user.

[0032] The adjustable illuminator of the present invention allows for an infinite amount of configurations that can be adapted for the targeted treatment area. The configurations may range from a flat-plane emitter (as shown in FIGS. 1B and 2B) to a substantially U-shaped configuration (as shown in FIGS. 1A and 2A). The adjustable illuminator may also be configured such that the two end panels 10a, 10e can be pulled back relative to the three middle panels 10b, 10c, 10d, such that a smaller U-shaped configuration may be created by the middle

panels. Thus, the adjustable illuminator allows for the treatment of additional areas of a patient's body. In other words, not only can the adjustable illuminator effectively deliver a uniform light intensity to traditional surfaces such as the face or scalp, but the adjustable illuminator can also provide a device that can easily be configured to treat other portions of a patient's body, in particular, those having smaller curved surfaces, such as the arms and legs. Moreover, the adjustable illuminator may also be easily positioned to deliver a uniform light intensity to larger treatment areas, such as the back or chest.

[0033] As described above, the narrower panels 10b, 10d are dimensioned such that the panels act as “lighted hinges.” Thus, when the wider panels 10a, 10c, 10e are adjusted into the desired form, the illuminator “bends” at the narrower panels 10b, 10d, where traditionally the “bend” would occur substantially at the hinge itself. Thus, instead of an unlighted “bent” portion as would occur in the conventional illuminator, the present illuminator provides a “bent” portion that is also configured to emit light, thereby helping to reduce optical dead space without requiring large amounts of power differentiation among the light sources of each panel to provide the required fill-in light. The effects of this configuration can be best seen in a comparison of FIGS. 7 and 8. FIG. 7 illustrates the light uniformity produced by a conventional illuminator, measured with a cosine response detector, which mimics the response of a patient's skin to the incident of light as described above, at a distance of two inches. Total light dose, in terms of J/cm^2 , was measured based on emitted irradiance (W/cm^2) over time (in seconds). The targeted treatment area shown is a patient's head, where height is shown as the y-axis and rotation angle from the center of the emitting surface is shown as the x-axis. As can be seen in FIG. 7, higher light doses of about $10 \text{ J}/\text{cm}^2$ occur at the center of the face (for example, at region A), near the patient's nose, where the patient is facing closest to, and substantially perpendicular to, the middle-most panel. Total light dose then begins to drop as movement away from the center of the face occurs where the effects of cosine “fall-off” and optical dead spaces are more prevalent. For example, light dose is reduced by about 20% at the patient's cheek areas (for example, at region B), and by about 80% toward the outer boundaries of the patient's face (for example, at region E), such as the ears and forehead. Thus, as shown in FIG. 7, conventional adjustable illuminators utilizing equally-sized panels operating at the same power output level produce a varying field of light uniformity, making it undesirable and ineffective for those treatments requiring highly specific light uniformity.

[0034] FIG. 8, on the other hand, illustrates the light uniformity produced by an embodiment of the present invention. The targeted treatment area is the same as that measured in FIG. 7. However, compared to FIG. 7, the light output uniformity produced by the illuminator is greatly enhanced across the patient's face and exhibits little to no deviation from the light output measured in the center of the patient's face to the light output measured at the edges of the patient's face. For example, as shown in FIG. 8, total light doses of about 10 J/cm^2 (for example, at region A') occur across all regions of the face, including the center of the face (for example, the patient's nose), the patient's cheek areas, and the outer boundaries of the patient's cheek areas, such as the ears and forehead. Moreover, total light dose drops off minimally (for example, at region B') at the extreme outer boundaries of the patient's face. In one embodiment, the measured output over the active emitting area (over the entire active emitting area) is within 60% of the measured maximum (over the entire active emitting area) measured with a cosine response detector over all operation distances. More preferably, the measured output over the emitting area is within 70% of the measured maximum over a distance of two and four inches. Even more preferably, the measured output over the emitting area is within 80% of the measured maximum over a distance of two and four inches.

[0035] One example of a treatment method for precancerous lesions, such as actinic keratosis, by PDT utilizing an adjustable illuminator described above in conjunction with ALA will now be described.

[0036] Essentially anhydrous ALA is admixed with a liquid diluent just prior to its use. The ALA admixture is topically applied to the lesions using a point applicator to control dispersion of the ALA admixture. After the initial application of the ALA admixture has dried, one or more subsequent applications may be similarly applied. Approximately 2 mg/cm^2 of ALA is administered. Formation of photosensitive porphyrin and photosensitization of the treated lesions occurs over the next 14-18 hours, during which time exposure to direct sunlight or other bright light sources should be minimized. Between 14 and 18 hours after administration of the ALA, the lesions are irradiated by the adjustable illuminator according to the present invention. The illuminator irradiates the lesions with a uniform blue light for a prescribed period. According to a preferred treatment, the visible light has a nominal wavelength of 417 nm. The illuminator may irradiate the lesions with a uniform red light for a prescribed period. In certain

embodiments, the illuminator irradiates the lesions with a uniform blue light for a first prescribed period and then irradiates the lesions with a uniform red light for a second prescribed period. For example, in some embodiments, the illuminator is configured to irradiate the lesions with a uniform blue light (e.g., 417 nm) at a low intensity (e.g., about 0.1 J/cm^2 to about 2 J/cm^2) to photobleach, for example, protoporphyrin IX (PpIX) present at the surface of the patient's skin, and irradiate the lesions with a uniform red light (e.g., 635 nm) at a high intensity (e.g., about 30 J/cm^2 to about 150 J/cm^2) to activate PpIX present at deeper layers of the patient's skin, thus avoiding potential damage to the upper layers of the patient's skin. The illuminator may be configured to simultaneously irradiate the patient's skin with the low intensity blue light and the high intensity red light or sequentially irradiate the patient's skin with the low intensity blue light and the high intensity red light. In certain embodiments, the illuminator is configured to irradiate the patient's skin with the low intensity blue light for about one hour to about three hours and irradiate the patient's skin with the high intensity red light for about 20 minutes to about 30 or 40 minutes, either at the same time the patient's skin is irradiated with the low intensity blue light or after the patient's skin has been irradiated with the low intensity blue light.

[0037] The invention thus provides a method for photodynamically diagnosing or treating a contoured surface of a patient, which includes providing the adjustable illuminator described above, placing the patient in the illuminator, and illuminating the patient to diagnose or treat the patient. The patient may be illuminated to treat actinic keratosis, acne, photo-damaged skin, cancer, warts, psoriasis, or other dermatological conditions. The method may also be used to remove hair and diagnose cancer.

[0038] Since the total light dose (J/cm^2) is equal to irradiance (W/cm^2) multiplied by time (sec), the only additional parameter that needs to be controlled for delivery of the correct treatment light dose is exposure time. This may be accomplished by the timer described above, which can control the electrical power supplied to the LED arrays 60 appropriately, and which can be set by the physician. Data has shown that 10 J/cm^2 delivered from a source with an irradiance density of 10 mW/cm^2 , or an irradiance density of about 9.3 to about 10.7 mW/cm^2 , produces clinically acceptable results for desired treatment areas (e.g., face, scalp, extremities). From the equation above, this light dose will require an exposure time of 1000 seconds (16 min. 40 sec). In addition, due to the addressable nature of the adjustable illuminator, the illuminator

may be used to treat a patient at higher power such that less time is required for effective treatment. For example, the adjustable illuminator may deliver an irradiance density of 20 mW/cm² for an exposure time of 500 seconds (8 min. 20 sec) to deliver a clinically acceptable light dose of 10 J/cm². Alternatively, the adjustable illuminator may include higher power ranges, such as 30 mW/cm², over an exposure time resulting in a light dose of 10 J/cm². A selected light dose may also be administered by additionally or alternatively varying the irradiance density over treatment time.

[0039] Additional advantages and modifications will readily occur to those skilled in the art. Therefore, the invention in its broader aspects is not limited to the specific details and representative devices and methods, shown and described herein. Accordingly, various modifications may be made without departing from the spirit and scope of the general inventive concept as defined by the appended claims and their equivalents.

WHAT IS CLAIMED IS:

1. A system for photodynamically diagnosing or treating a patient, comprising:
an illuminator comprising at least five panels connected by nested hinges configured to reduce optical dead space,
light sources disposed on a surface of the illuminator, the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources,
one of the at least five panels positioned as a center panel configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel.
2. The system of claim 1, wherein the illuminator is configured to uniformly illuminate the treatment surface when the treatment surface is at a distance of two to four inches from the illuminator.
3. The system of claim 1, wherein the illuminator is configured to output red light at an intensity of about 30 J/cm² to about 150 J/cm².
4. The system of claim 1, wherein the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm².
5. The system of claim 1, wherein a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm.
6. A method of photodynamically diagnosing or treating a patient, comprising:
positioning an illuminator proximate to the patient, the illuminator comprising at least five panels connected by nested hinges configured to reduce optical dead space; and
uniformly illuminating a treatment surface of the patient with the illuminator.
7. The method of claim 6, wherein the nested hinges are mounted to inner side surfaces of adjacent panels.

8. The method of claim 6, wherein output of the illumination over an active emitting area is within 60% of maximum over all operation distances.
9. The method of claim 6, wherein output of the illumination over an active emitting area is within 70% of maximum over a distance of two and four inches.
10. The method of claim 6, wherein output of the illumination over an active emitting area is within 80% of maximum over a distance of two and four inches.
11. The method of claim 6, further comprising determining a size of the treatment surface of the patient using a sensor.
12. The method of claim 6, further comprising determining a shape of the treatment surface of the patient using a sensor.
13. The method of claim 6, wherein at least one panel includes tabs outwardly extending from a top side and a bottom side, the tabs being configured to receive an adjacent panel therein.
14. The method of claim 11, further comprising adjusting an overall light dose with a controller based on the determined size of the treatment surface.
15. The method of claim 12, further comprising adjusting an overall light dose with a controller based on the determined shape of the treatment surface.
16. The method of claim 11, further comprising adjusting positioning of panels with at least one actuator based on the determined size of the treatment surface.
17. The method of claim 12, further comprising adjusting positioning of panels with at least one actuator based on the determined shape of the treatment surface.
18. The method of claim 6, further comprising changing intensities of light sources of the illuminator with a controller in accordance with information received from at least one sensor relating to a curvature of the treatment surface.
19. The method of claim 6, wherein at least one panel includes a recess configured to receive a flange of a nested hinge.

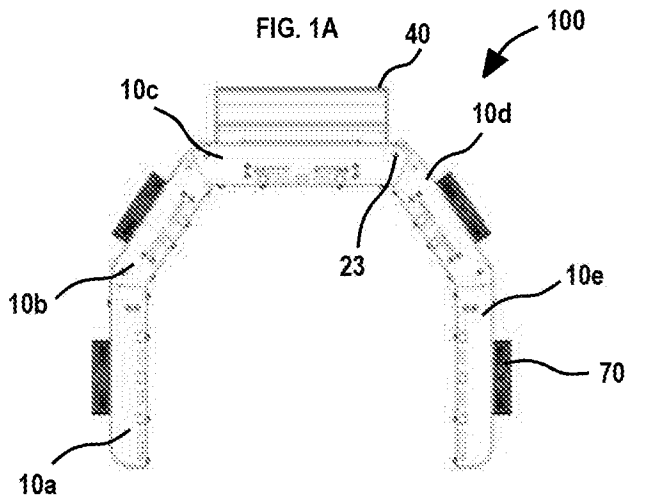
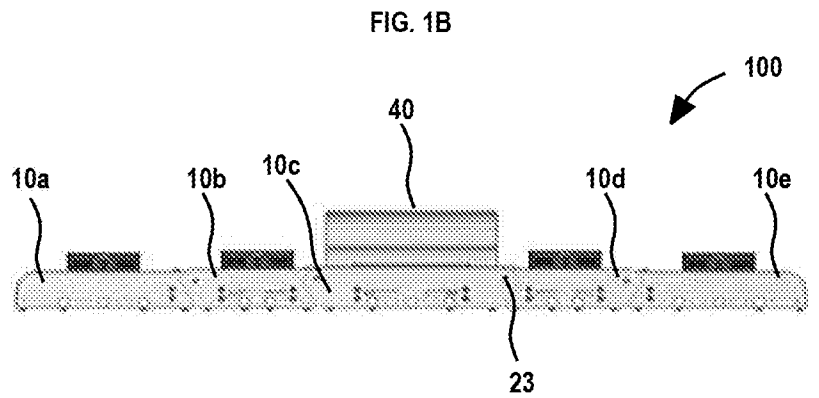
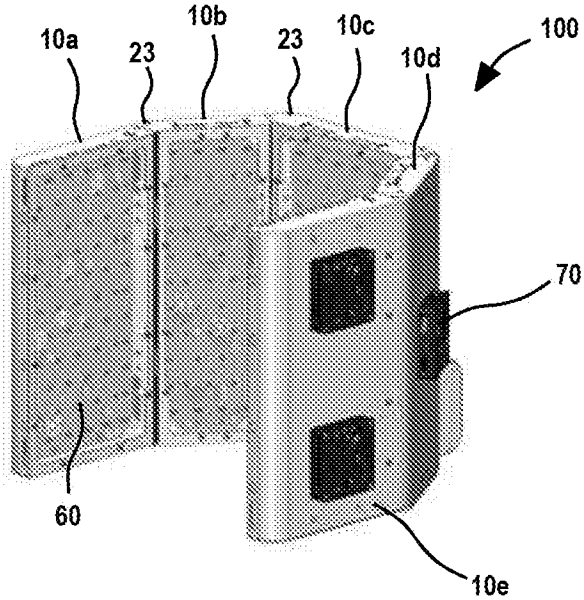
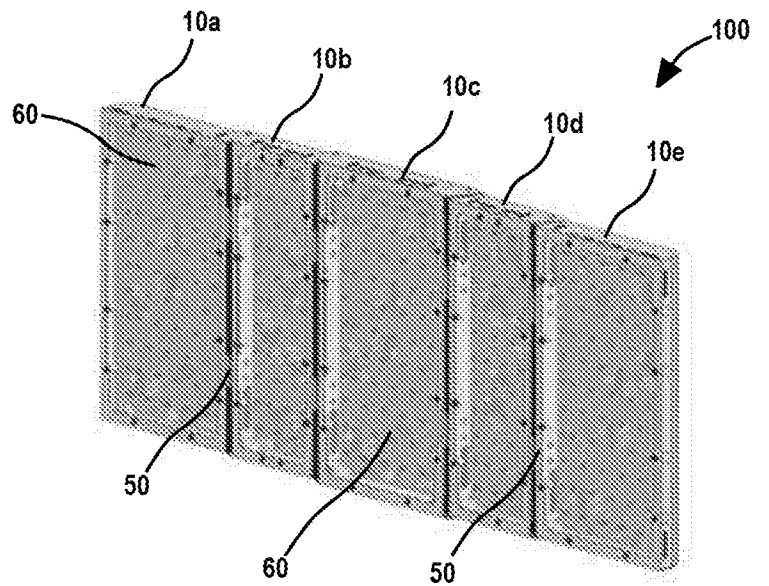
20. The method of claim 6,

wherein the illuminator comprises at least three first panels having first widths, at least two second panels having second widths, wherein each of the second widths of the at least two second panels is narrower than each of the first widths of the at least three first panels; and

wherein the at least three first panels and the at least two second panels are connected in an alternative manner such that each of the at least two second panels has a first lateral side connected to a respective one of the at least three first panels and a second lateral side connected to another respective one of the at least three first panels.

ABSTRACT

An adjustable illuminator for photodynamically diagnosing or treating a surface includes a plurality of first panels and at least one second panel. The plurality of first panels have wider widths and the at least one second panel has a narrower width. The narrower width is less than the wider widths. The illuminator further includes a plurality of light sources, each mounted to one of the plurality of first panels or the at least one second panel and configured to irradiate the surface with substantially uniform intensity visible light. The plurality of first panels and the at least one second panel are rotatably connected. The at least one second panel is connected on each side to one of the plurality of first panels. The second panel acts as a “lighted hinge” to reduce or eliminate optical dead spaces between adjacent panels when the illuminator is bent into a certain configuration.



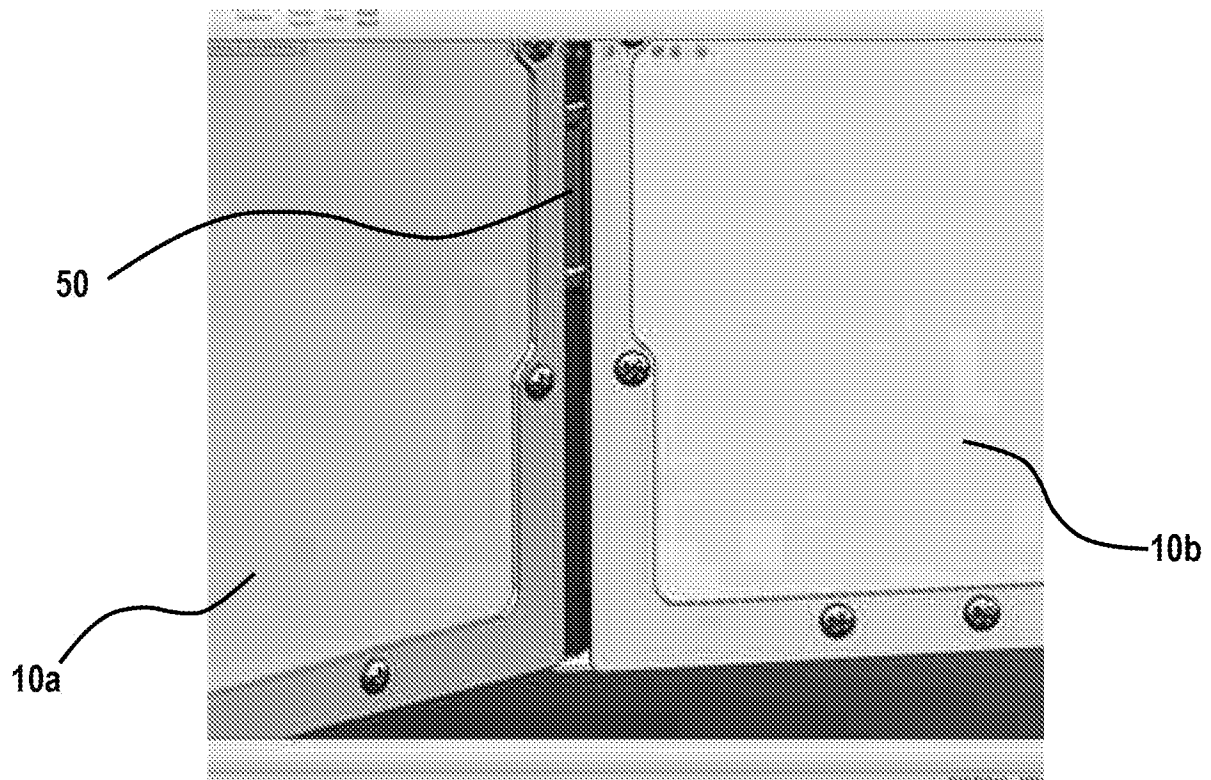


FIG. 3A

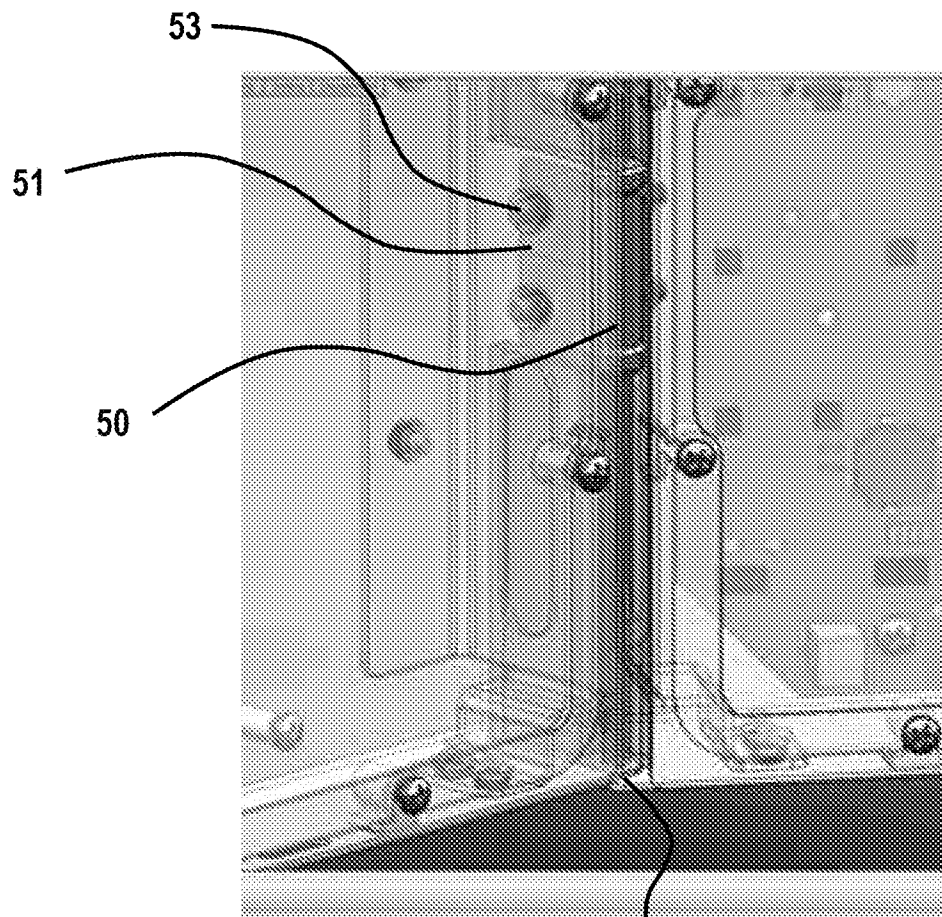


FIG. 3B

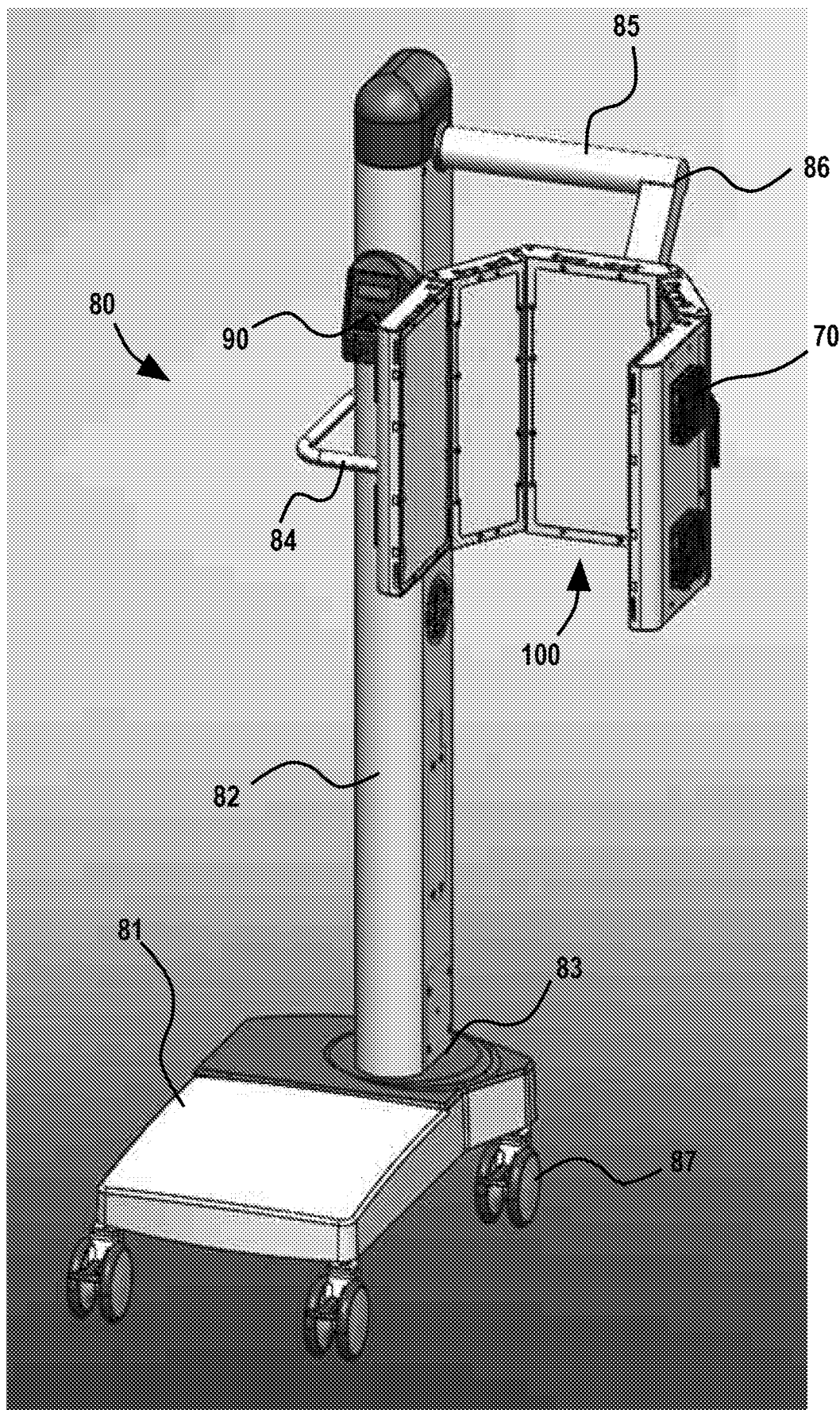


FIG. 4

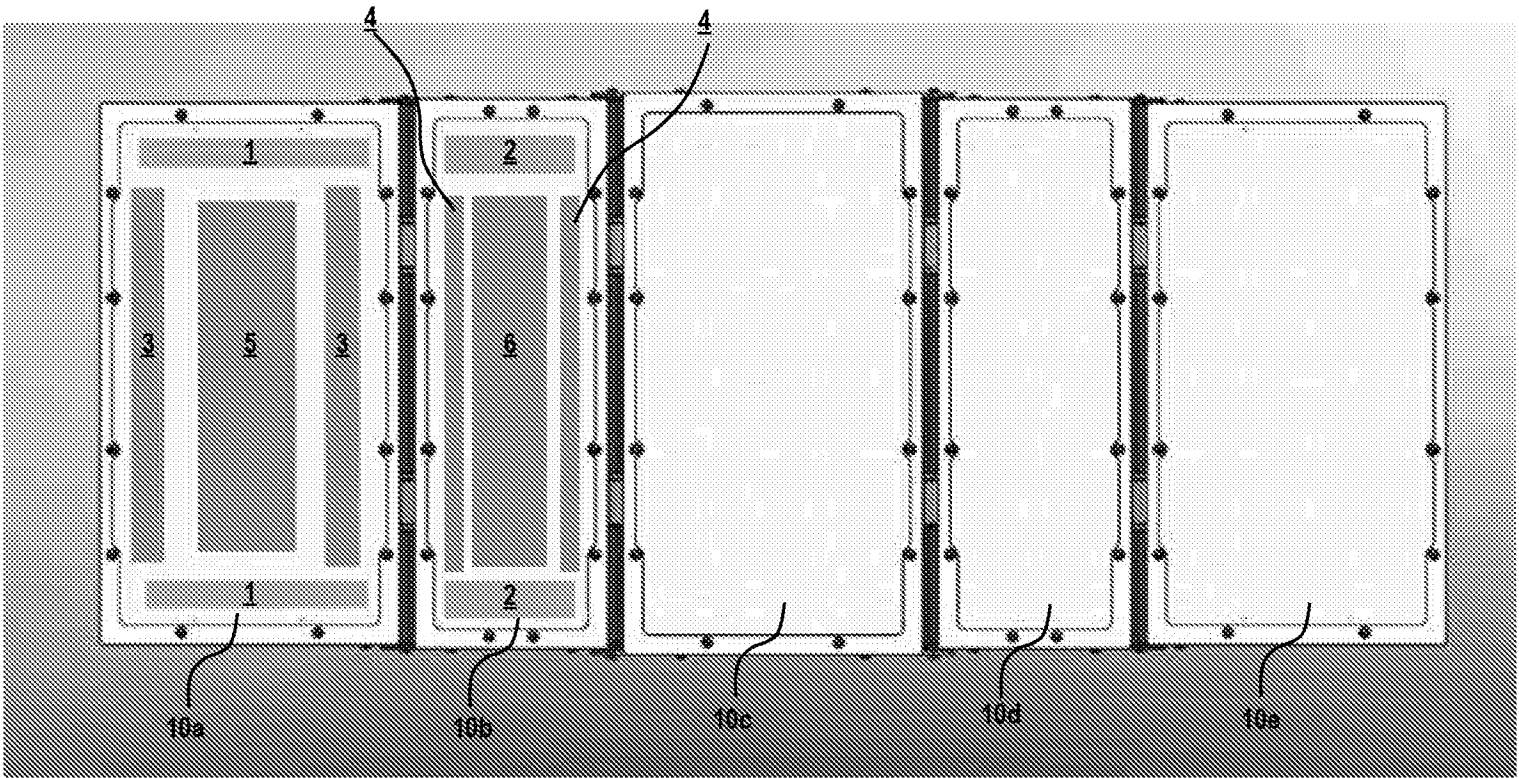


FIG. 5

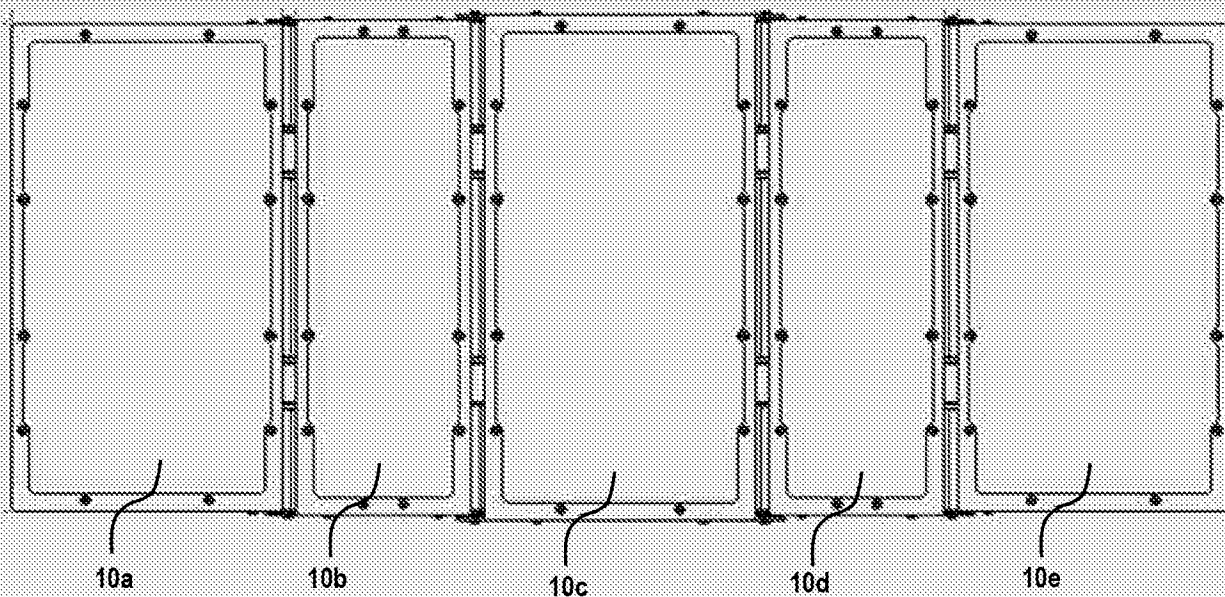


FIG. 6

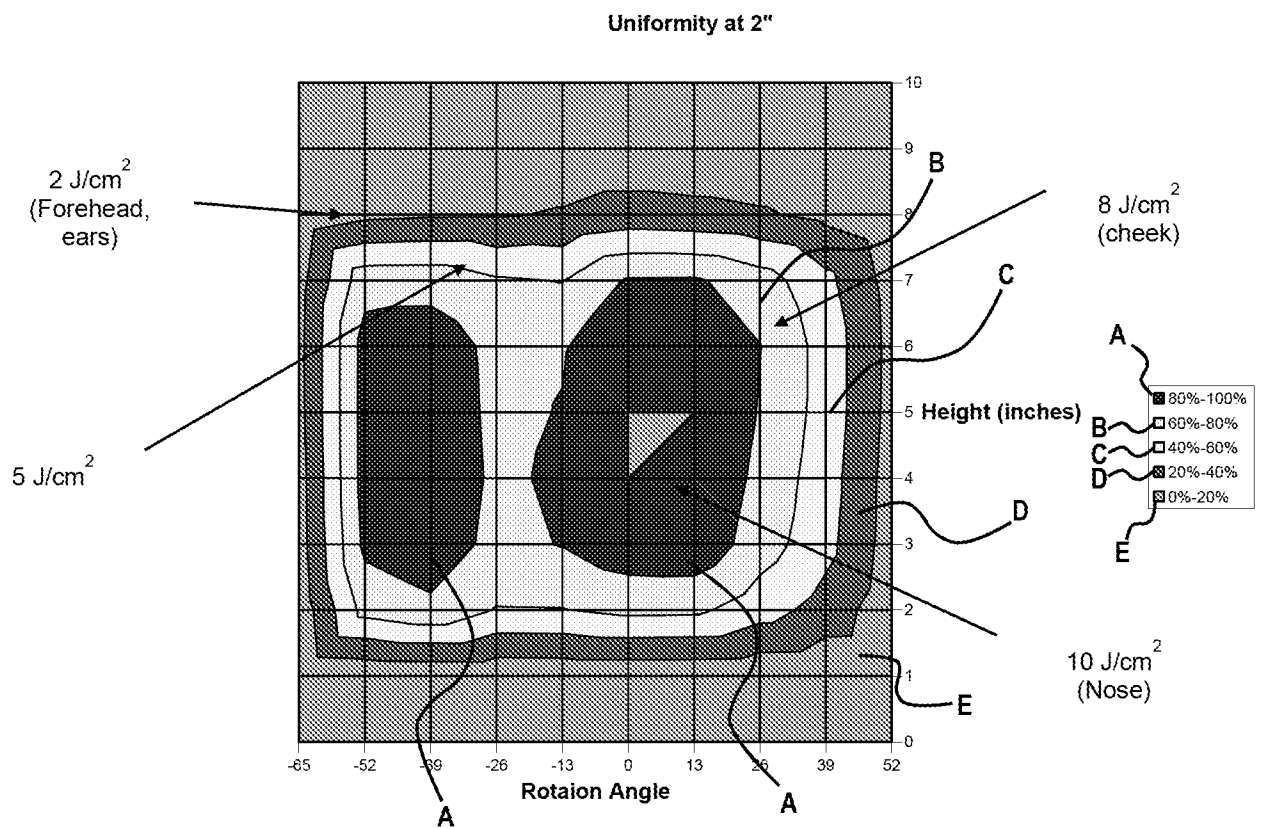


FIG. 7

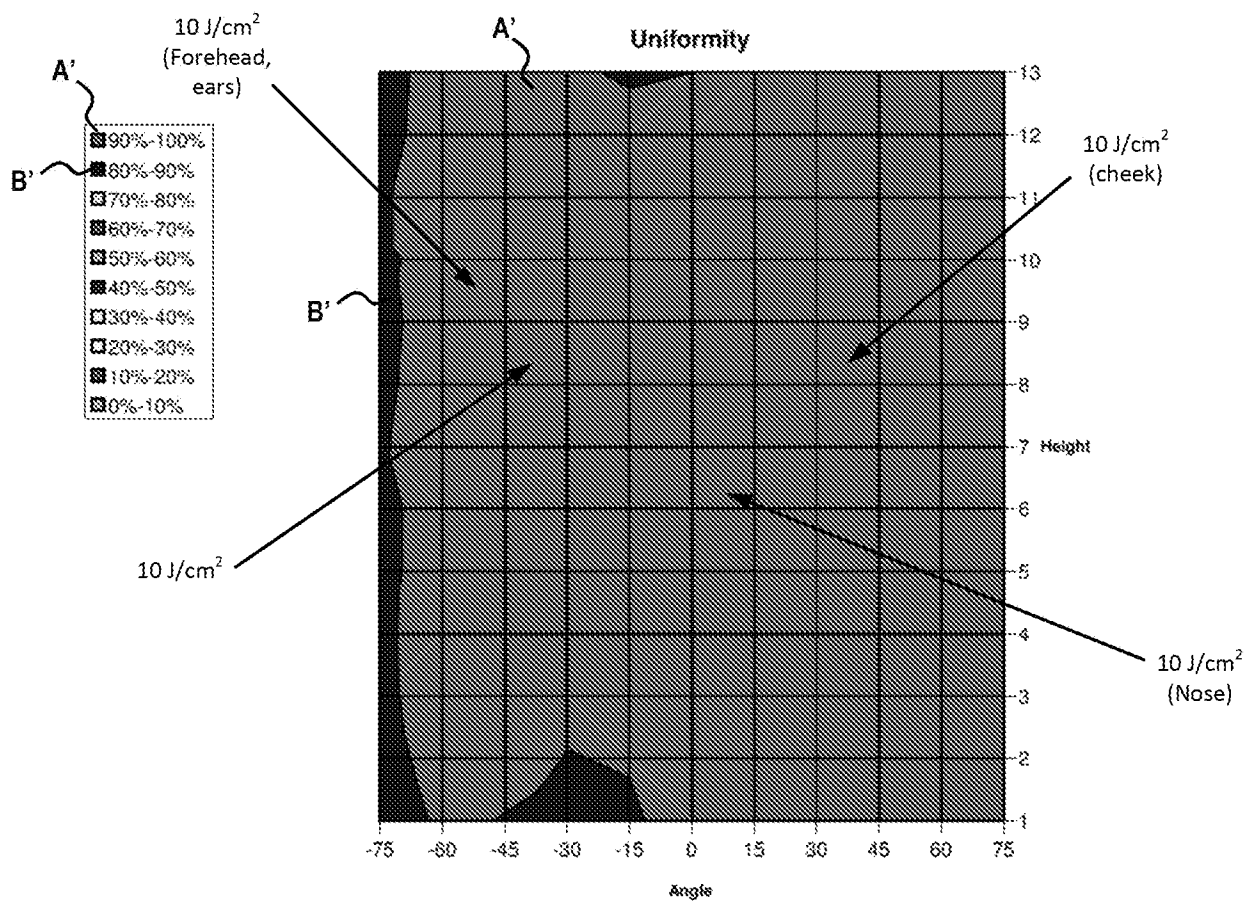


FIG. 8

**DECLARATION FOR UTILITY OR
DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

☐ Declaration Submitted With Initial Filing

OR

☒ Declaration Submitted After Initial Filing
(surcharge (37 CFR 1.16(f)) required)

Attorney Docket Number	067286-0395
First Named Inventor	Thomas BOYAJIAN
COMPLETE IF KNOWN	
Application Number	15/292,731
Filing Date	10/13/2016
Art Unit	Unassigned
Examiner Name	Unassigned

ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

(Title of the Invention)

As a below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application,

OR

☒ United States Application Number or PCT International application number 15/292,731 filed on 10/13/2016.

The above-identified application was made or authorized to be made by me.

I believe I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

Authorization To Permit Access To Application by Participating Office

☐ If checked, the undersigned hereby grants the USPTO authority to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the World Intellectual Property Office (WIPO), and any other intellectual property offices in which a foreign application claiming priority to the above-identified patent application is filed access to the above-identified patent application. See 37 CFR 1.14(c) and (h). This box should not be checked if the applicant does not wish the EPO, JPO, KIPO, WIPO, or other intellectual property office in which a foreign application claiming priority to the above-identified patent application is filed to have access to the above-identified patent application.

In accordance with 37 CFR 1.14(h)(3), access will be provided to a copy of the above-identified patent application with respect to: 1) the above-identified patent application-as-filed; 2) any foreign application to which the above-identified patent application claims priority under 35 U.S.C. 119(a)-(d) if a copy of the foreign application that satisfies the certified copy requirement of 37 CFR 1.55 has been filed in the above-identified patent application; and 3) any U.S. application-as-filed from which benefit is sought in the above-identified patent application.

In accordance with 37 CFR 1.14(c), access may be provided to information concerning the date of filing the Authorization to Permit Access to Application by Participating Offices.

DECLARATION — Utility or Design Patent Application

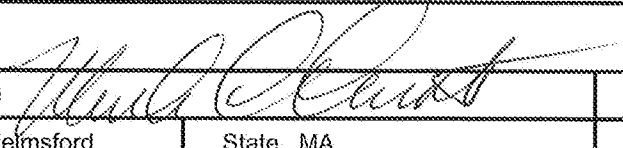
Docket Number: 067286-0395

Application No: 15/292,731

Direct all correspondence to:	☒ The address associated with Customer Number:	22428	OR ☐	Correspondence address below
Name				
Address				
City	State	Zip		
Country	Telephone	Email		
<p align="center">WARNING:</p> <p>Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available. Petitioner/applicant is advised that documents which form the record of a patent application (such as the PTO/SB/01) are placed into the Privacy Act system of records DEPARTMENT OF COMMERCE, COMMERCE-PAT-7, System name: <i>Patent Application Files</i>. Documents not retained in an application file (such as the PTO-2038) are placed into the Privacy Act system of COMMERCE/PAT-TM-10, System name: <i>Deposit Accounts and Electronic Funds Transfer Profiles</i>.</p>				
LEGAL NAME OF SOLE OR FIRST INVENTOR:				
(E.g., Given Name (first and middle (if any)) and Family Name or Surname)				
Thomas BOYAJIAN				
Inventor's Signature		Date (optional)		
Residence: City Wilmington	State MA		Country U.S.A.	
Mailing Address				
c/o DUSA Pharmaceuticals, Inc., 25 Upton Drive				
City Wilmington	State Massachusetts	Zip 01887	Country United States of America	
☒ Additional inventors are being named on the _____ supplemental sheet(s) PTO/AIA/10 attached hereto				

**SUPPLEMENTAL SHEET FOR
DECLARATION**
ADDITIONAL INVENTOR(S)
 Supplemental Sheet (for PTO/AIA/08,09)

Page ___ of ___

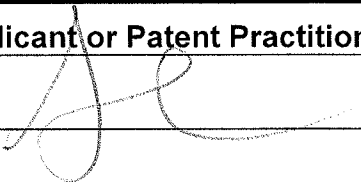
Legal Name of Additional Joint Inventor, if any:			
(E.g., Given Name (first and middle (if any)) and Family Name or Surname)			
Mark CAROTA			
Inventor's Signature 		Date (optional)	
Residence: City Chelmsford	State MA	Country U.S.A.	
Mailing Address			
C/o DUSA Pharmaceuticals, Inc. 25 Upton Drive			
City Wilmington	State Massachusetts	Zip 01887	Country United States of America
Legal Name of Additional Joint Inventor, if any:			
(E.g., Given Name (first and middle (if any)) and Family Name or Surname)			
Brian MAZEJKA			
Inventor's Signature 		Date (optional)	
Residence: City Salem	State NH	Country U.S.A.	
Mailing Address			
c/o DUSA Pharmaceuticals, Inc., 25 Upton Drive			
City Wilmington	State Massachusetts	Zip 01887	Country United States of America

TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

Application Number	Unassigned
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Title	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	067286-0410

SIGNATURE of Applicant or Patent Practitioner

Signature		Date (Optional)	2/14/2020
Name	Glenn Law	Registration Number	34,371
Title (if Applicant is a juristic entity)	Attorney for Applicant		
Applicant Name (if Applicant is a juristic entity)	DUSA PHARMACEUTICALS, INC.		

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.



*Total of 1 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.

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

(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: 22428
- 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: 22428

OR

Firm or Individual Name				
Address				
City	State	Zip		
Country				
Telephone	Email			

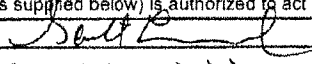
I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

DUSA PHARMACEUTICALS, 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 1.45(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)	
Name	Scott Lundahl		
Title	VP Regulatory Affairs & Intellectual Property		

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 _____ 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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: Unassigned
Filing Date: 2/14/2020
Examiner: Unassigned
Art Unit: Unassigned
Confirmation No.: Unassigned

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

Applicant requests that, in accordance with 37 CFR §1.98(d), the Examiner review all applications relied on for an earlier effective filing date under 35 U.S.C. 120, including Application No. 15/292,731, filed 10/13/2016, for copies of references of record therein that are not being provided here.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

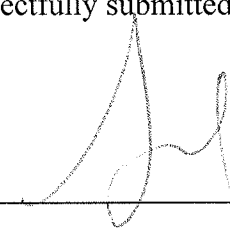
CONCISE EXPLANATION OF RELEVANCE

The relevance of the documents listed on the attached PTO Form SB08 can be found in the parent application.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 14, 2020

By 

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known	
Sheet 1 of 3		Application Number		Unassigned	
		Filing Date		2/14/2020	
		First Named Inventor		Thomas BOYAJIAN	
		Art Unit		Unassigned	
		Examiner Name		Unassigned	
		Attorney Docket Number		067286-0410	

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)			
	A1	5,814,008	09-29-1998	CHEN ET AL.	
	A2	5,849,027	12-15-1998	GART ET AL.	
	A3	6,223,071-B1	04-24-2001	LUNDAHL ET AL.	
	A4	6,709,446-B2	03-23-2004	LUNDAHL ET AL.	
	A5	7,156,865-B2	01-02-2007	WALDMANN, GERHARD	
	A6	7,190,109-B2	03-13-2007	LUNDAHL ET AL.	
	A7	7,723,910-B2	05-25-2010	LUNDAHL ET AL.	
	A8	8,030,836-B2	10-04-2011	LUNDAHL ET AL.	
	A9	8,216,289-B2	07-10-2012	LUNDAHL ET AL.	
	A10	8,758,418-B2	06-24-2014	LUNDAHL ET AL.	
	A11	9,108,045-B2	08-18-2015	SAKAMOTO ET AL.	
	A12	9,533,170-B2	01-03-2017	DYE ET AL.	
	A13	2003/0088296-A1	05-08-2003	WALDMANN, GERHARD	
	A14	2004/0162596-A1	08-19-2004	ALTSHULER ET AL.	
	A15	2004/0260365-A1	12-23-2004	GROSETH ET AL.	
	A16	2005/0075703-A1	04-07-2005	LARSEN, ERIC	
	A17	2005/0090877-A1	04-28-2005	HARTH ET AL.	
	A18	2006/0241726-A1	10-26-2006	WHITEHURST, COLIN	
	A19	2006/0253175-A1	11-09-2006	FAN ET AL.	
	A20	2006/0287696-A1	12-21-2006	WRIGHT ET AL.	
	A21	2007/0283655-A1	12-13-2007	TOBIN, STEPHEN M.	
	A22	2008/0031924-A1	02-07-2008	GILSON ET AL.	
	A23	2010/0010591-A1	01-14-2010	DAFFER, STEVEN J.	
	A24	2010/0174223-A1	07-08-2010	SAKAMOTO ET AL.	
	A25	2011/0106222-A1	05-05-2011	WILSON ET AL.	
	A26	2012/0283328-A1	11-08-2012	MODI, PANKAJ	
	A27	2012/0287671-A1	11-15-2012	PARKER ET AL.	
	A28	2013/0066405-A1	03-14-2013	DOUGAL, GORDON REX PATERSON	
	A29	2013/0190845-A1	07-25-2013	LIU ET AL.	
	A30	2014/0067024-A1	03-06-2014	JONES ET AL.	
	A31	2015/0162109-A1	06-11-2015	NAGER, ZACHARY	
	A32	2015/0238776-A1	08-27-2015	SAKAMOTO ET AL.	
	A33	2016/0166846-A1	06-16-2016	CHAE, HIUN SUK	
	A34	2016/0175609-A1	06-23-2016	DYE ET AL.	
	A35	2016/0175610-A1	06-23-2016	LIVINGSTON ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

Examiner Signature		Date Considered	
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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	Unassigned
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	Unassigned
Examiner Name	Unassigned				
Sheet	2	of	3	Attorney Docket Number	067286-0410

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	A36	EP-1 238 652-A1	09-11-2002	COSMO OIL CO LTD		
	A37	WO-02/13788-A1	02-21-2002	GEN HOSPITAL CORP		
	A38	WO-2007/112427-A2	10-04-2007	TOBIN, STEPHEN M.		
	A39	WO-2009/003173-A1	12-31-2008	THE GENERAL HOSPITAL CORPORATION		ABS
	A40	WO-2011/124912-A1	10-13-2011	DOUGAL, GORDON REX, PATTERSON		
	A41	WO-2014/131115-A1	09-04-2014	KLOX TECHNOLOGIES INC [CA]		ABS
	A42	WO-2015/041919-A1	03-26-2015	D-REV: DESIGN FOR THE OTHER NINETY PERCENT		
	A43	WO-99/22802-A1	05-14-1999	DUSA PHARMACEUTICALS INC [CA]		

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 ⁶
	A44	Australian Office Action, Application No. 2019200152, 11/11/2019, 9 pages	
	A45	European Office Action, Application No. 16787667.1, 9/24/2019, 5 pages	
	A46	GLAD.com.au: "GLAD History", 2012, [online] URL: http://www.glad.com.au/about-glad/glad-history/ , retrieved online 8 November 2019	
	A47	International Preliminary Report on Patentability, PCT/US2016/056572, April 26, 2018, 9 pages	
	A48	International Preliminary Report on Patentability, PCT/US2018/027070, 10/24/2019, 10 pages	
	A49	Notice of Allowance, 15/487,991 (067286-0398), 01/15/2020, 11 pages	
	A50	Notice of Allowance, 15/487,991 (067286-0398), 10/02/2019, 16 pages	
	A51	International Search Report and Written Opinion International Application No. PCT/US2018/027070, October 16, 2018, 18 pages	
	A52	Partial International Search, Annex to Form PCT/ISA/206, International Application No. PCT/US2018/027070, July 19, 2018, 10 pages	
	A53	USPTO Advisory Action, 15/487,991, 5/15/2018 (067286-0398), 5 pages	

Examiner Signature		Date Considered	
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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known			
				Application Number		Unassinged	
				Filing Date		2/14/2020	
				First Named Inventor		Thomas BOYAJIAN	
				Art Unit		Unassinged	
				Examiner Name		Unassinged	
Sheet	3	of	3	Attorney Docket Number		067286-0410	

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 ⁶
	A54	USPTO Interview Summary, 15/487,991 (067286-0398), 9/22/2017, 4 pages		
	A55	USPTO Notice of Allowance, 15/292,731 (067286-0395), 11/14/2019, 12 pages		
	A56	USPTO Office Action, 15/487,991 (067286-0398), 07/31/2018, 20 pages		
	A57	USPTO Office Action, 15/487,991 (067286-0398), 04/09/2019, 27 pages		
	A58	USPTO Office Action, 15/487,991 (067286-0398), 06/12/2017, 22 pages		
	A59	USPTO Office Action, 15/487991 (067286-0398), 2/6/2018, 19 pages		

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

Electronic Patent Application Fee Transmittal

Application Number:				
Filing Date:				
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS			
First Named Inventor/Applicant Name:	Thomas BOYAJIAN			
Filer:	Glenn Law/Effie Hale			
Attorney Docket Number:	067286-0410			
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	300	300
UTILITY SEARCH FEE	1111	1	660	660
UTILITY EXAMINATION FEE	1311	1	760	760
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				1720

Electronic Acknowledgement Receipt

EFS ID:	38589990
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas BOYAJIAN
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	14-FEB-2020
Filing Date:	
Time Stamp:	12:14:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$ 1720
RAM confirmation Number	E20202DC15400972
Deposit Account	190741
Authorized User	Effie Hale

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:
37 CFR 1.16 (National application filing, search, and examination fees)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal of New Application	DivTransmittal.pdf	217946	no	3
			9efcf3bf254540caff3de2fe1024e88fd74dd37a		
Warnings:					
Information:					
2	Application Data Sheet	ADS.pdf	982259	no	8
			34633fbba09a3645bcb0d95fe0c142efd9d2ae0a		
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3		DivSpec.pdf	136125	yes	18
			3ab36b1f5c13a937797c83ecab120e95cb4dd408		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Specification		1	14	
	Claims		15	17	
	Abstract		18	18	
Warnings:					
Information:					
4	Drawings-only black and white line drawings	Drwgs.pdf	2186856	no	7
			6366da4bd046992e03b6ac7e18a78e67ab2a6a29		
Warnings:					
Information:					

5	Oath or Declaration filed	Declaration.pdf	4353771	no	3
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Warnings:					
Information:					
6	Power of Attorney	PoA.pdf	345719	no	2
			ca572fb969f68aec50b11b97b909e2a95b16cd1b		
Warnings:					
Information:					
7	Transmittal Letter	IDSTrans.pdf	166139	no	2
			2c02b69d5470e5b5cc8727b79ad8a3a77223740c		
Warnings:					
Information:					
8	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	122277	no	3
			ce326899be27cf778348a76e1bd6728a4ceffc1bb		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
9	Fee Worksheet (SB06)	fee-info.pdf	34971	no	2
			931f35773af0c5824346caf4563ca7d9ddfca8c9		
Warnings:					
Information:					
Total Files Size (in bytes):			8546063		

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.

SCORE Placeholder Sheet for IFW Content

Application Number: 16791004

Document Date: 02/14/2020

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Drawing

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- USPTO employees may access SCORE content via DAV or via the SCORE web page.
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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
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/791,004	02/14/2020	Thomas Boyajian	067286-0410

CONFIRMATION NO. 2631

FORMALITIES LETTER



OC000000115118571

22428
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Date Mailed: 03/04/2020

NOTICE TO FILE CORRECTED APPLICATION PAPERS

Filing Date Granted

An application number and filing date have been accorded to this application. The application is informal since it does not comply with the regulations for the reason(s) indicated below. Applicant is given **TWO MONTHS** from the date of this Notice within which to correct the informalities indicated below. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
 - The drawings must be made on paper that has a white background (see 37 CFR 1.84(e)). For example, drawings on graph paper, lined paper, or paper that has a non-white background are not acceptable. See Figure(s) 4-6.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice".
<https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html>

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at <http://www.uspto.gov/ebc>.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

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**.

/bzewdie/

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						Application or Docket Number 16/791,004				
APPLICATION AS FILED - PART I										
(Column 1)		(Column 2)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY				
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)		RATE(\$)	FEE(\$)			
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	300			
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A			N/A	660			
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	760			
TOTAL CLAIMS (37 CFR 1.16(j))	20	minus 20 = *			OR	x 100 =	0.00			
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2	minus 3 = *				x 460 =	0.00			
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).						0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00			
			TOTAL			TOTAL	1720			
* If the difference in column 1 is less than zero, enter "0" in column 2.										
APPLICATION AS AMENDED - PART II										
(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY		
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=	OR	x	=
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	
AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=	OR	x	=
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	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 found in the appropriate box in column 1.										



UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
16/791,004	02/14/2020	2875	1720	067286-0410	20	2

CONFIRMATION NO. 2631

FILING RECEIPT



0000000115118570

22428
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Date Mailed: 03/04/2020

Receipt is acknowledged of this non-provisional utility 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 FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

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Inventor(s)

Thomas Boyajian, Wilmington, MA;
Mark Carota, Chelmsford, MA;
Brian Mazejka, Salem, NH;

Applicant(s)

DUSA Pharmaceuticals, Inc., Wilmington, MA;

Assignment For Published Patent Application

DUSA Pharmaceuticals, Inc., Wilmington, MA

Power of Attorney: The patent practitioners associated with Customer Number 22428

Domestic Priority data as claimed by applicant

This application is a DIV of 15/292,731 10/13/2016 PAT 10589122
which claims benefit of 62/241,902 10/15/2015

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: Yes

Permission to Access Search Results: Yes

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: 03/02/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/791,004**

Projected Publication Date: To Be Determined - pending completion of Corrected Papers

Non-Publication Request: No

Early Publication Request: No
Title

ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

Preliminary Class

362

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).

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Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

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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).

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technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND DIAGNOSIS
Appl. No.: 16/791,004
Filing Date: 2/14/2020
Examiner: Unassigned
Art Unit: 2875
Confirmation No.: 2631

RESPONSE TO NOTICE TO FILE CORRECTED APPLICATION PAPERS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

This communication responds to the Notice to File Corrected Application Papers mailed March 4, 2020 in the captioned application and is timely filed within the two-month response period. A return copy of the Notice is enclosed.

The Notice indicates that replacement drawings are required because the drawings of record include drawings made on paper with a non-white background. The Notice refers to Figures 4-6 in particular.

Applicant submits herewith replacement drawings of Figures 1-8. Figures 1-8 have been replaced with formal line drawings having a white background. The amendments do not add new matter.

The replacement drawings are believed to resolve the issues noted in the Notice.
Acceptance of the drawings and favorable consideration are respectfully requested.

Although no fees are believed due, the Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741.

Respectfully submitted,

Date April 27, 2020

By /Kiri Lee Sharon/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Telephone: (202) 295-4092
Facsimile: (202) 672-5399

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828

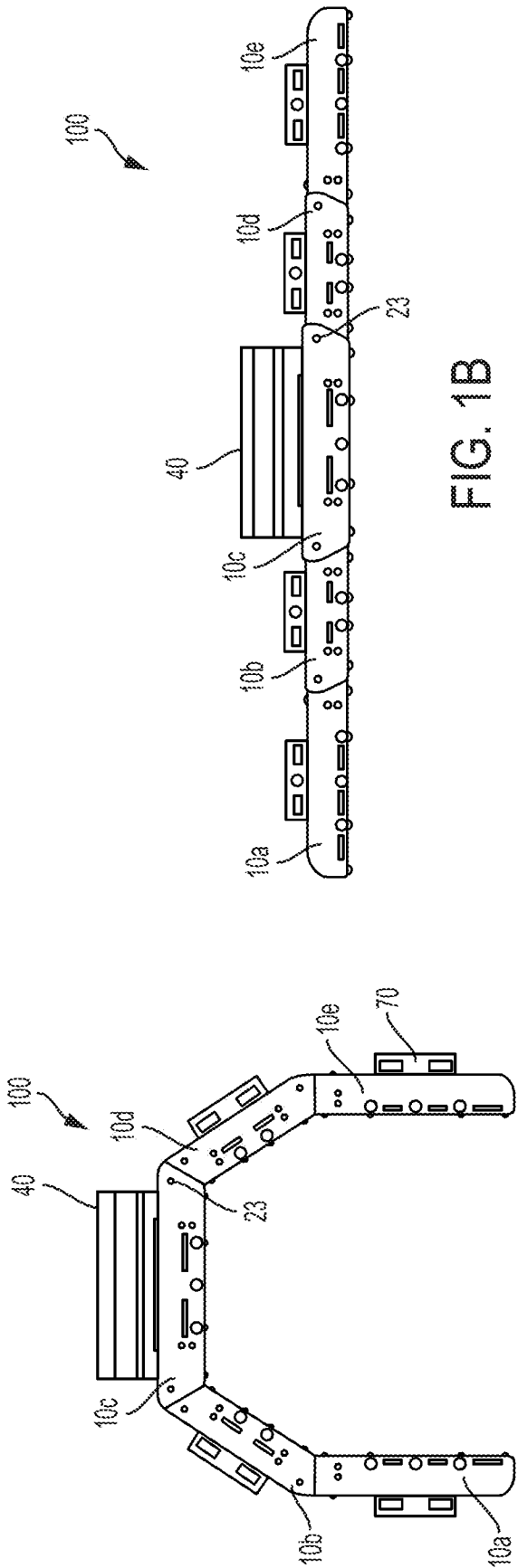


FIG. 1B

FIG. 1A

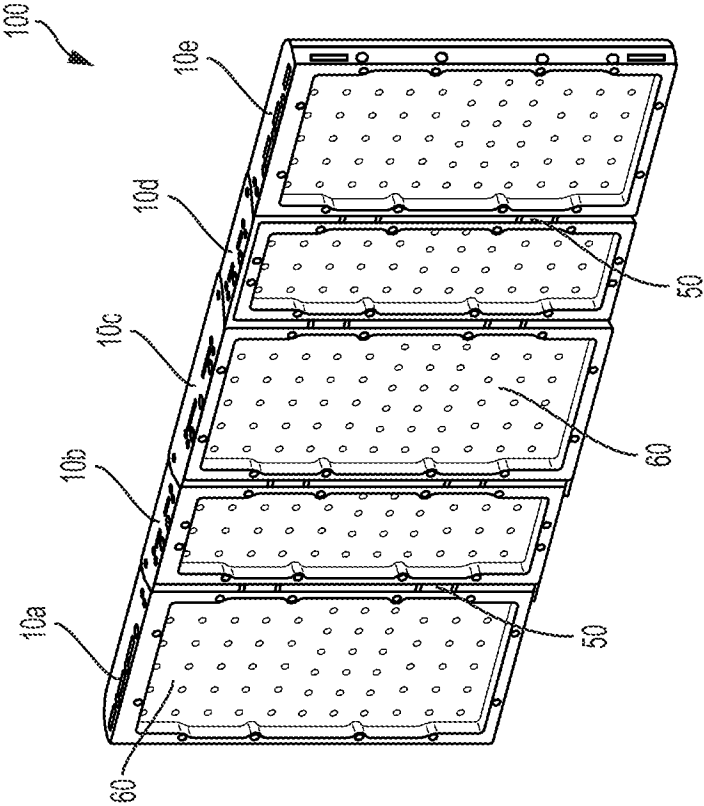


FIG. 2B

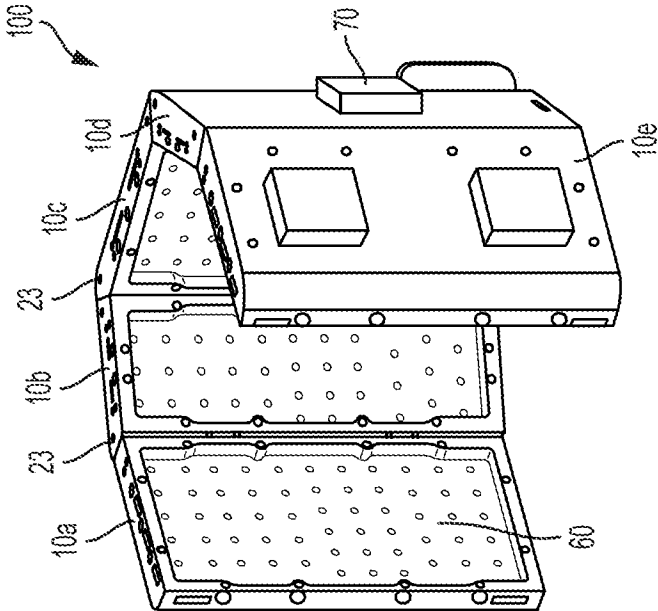


FIG. 2A

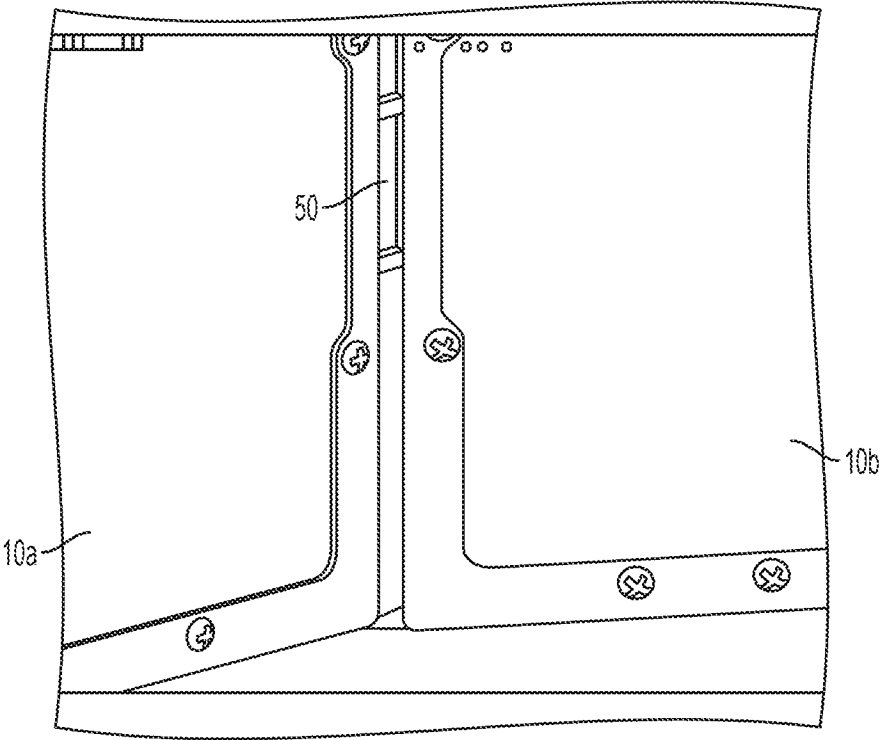


FIG. 3A

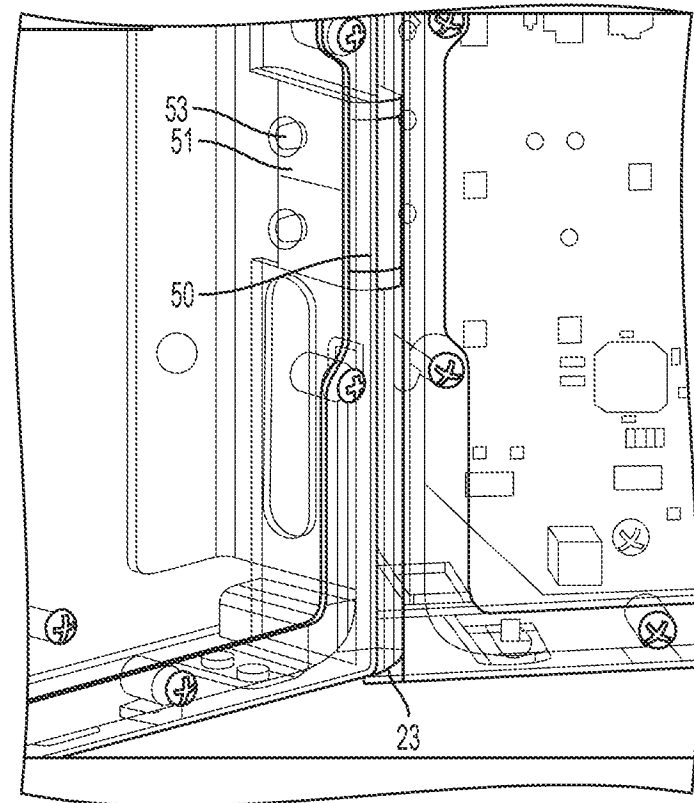


FIG. 3B

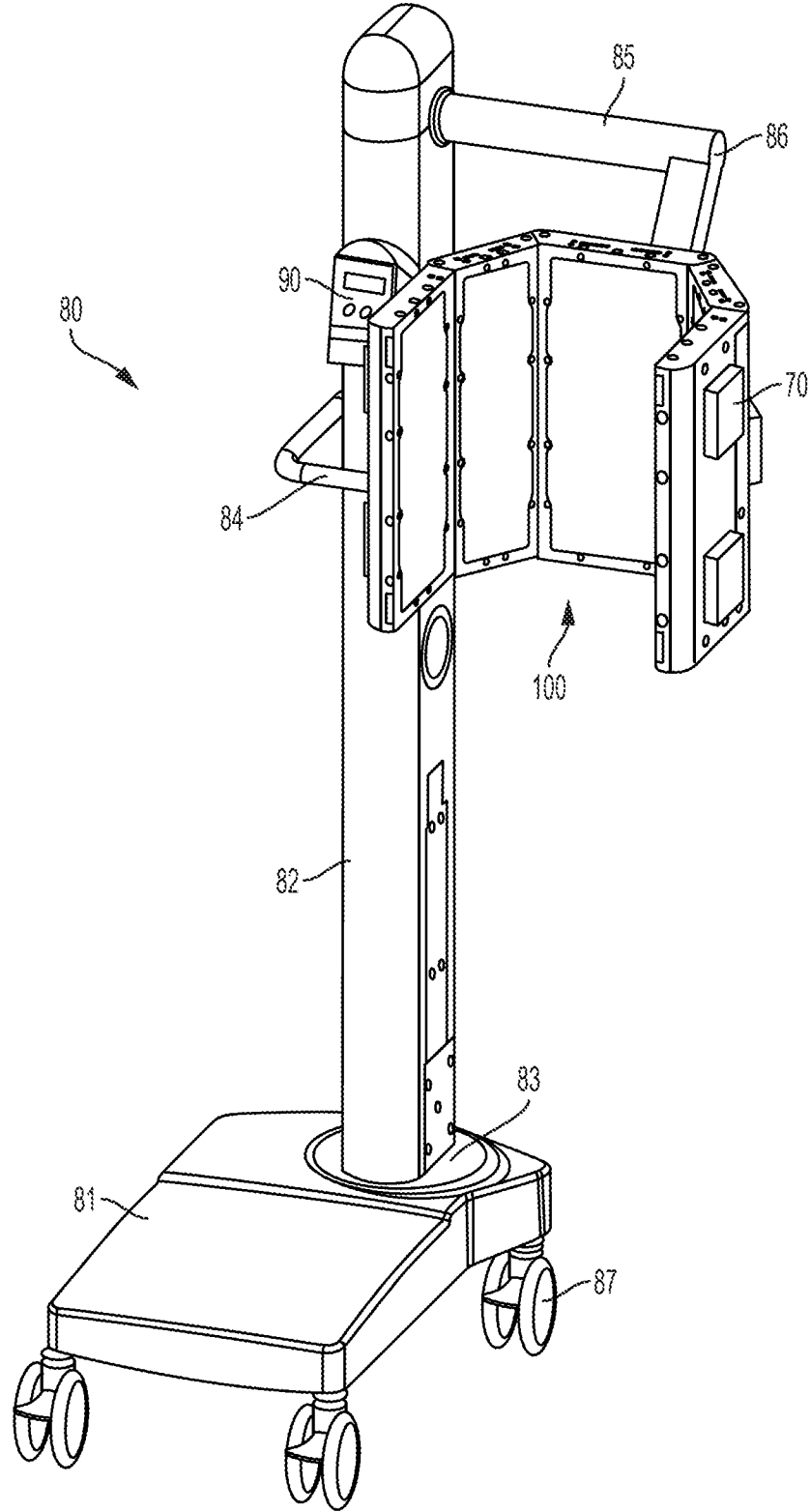


FIG. 4

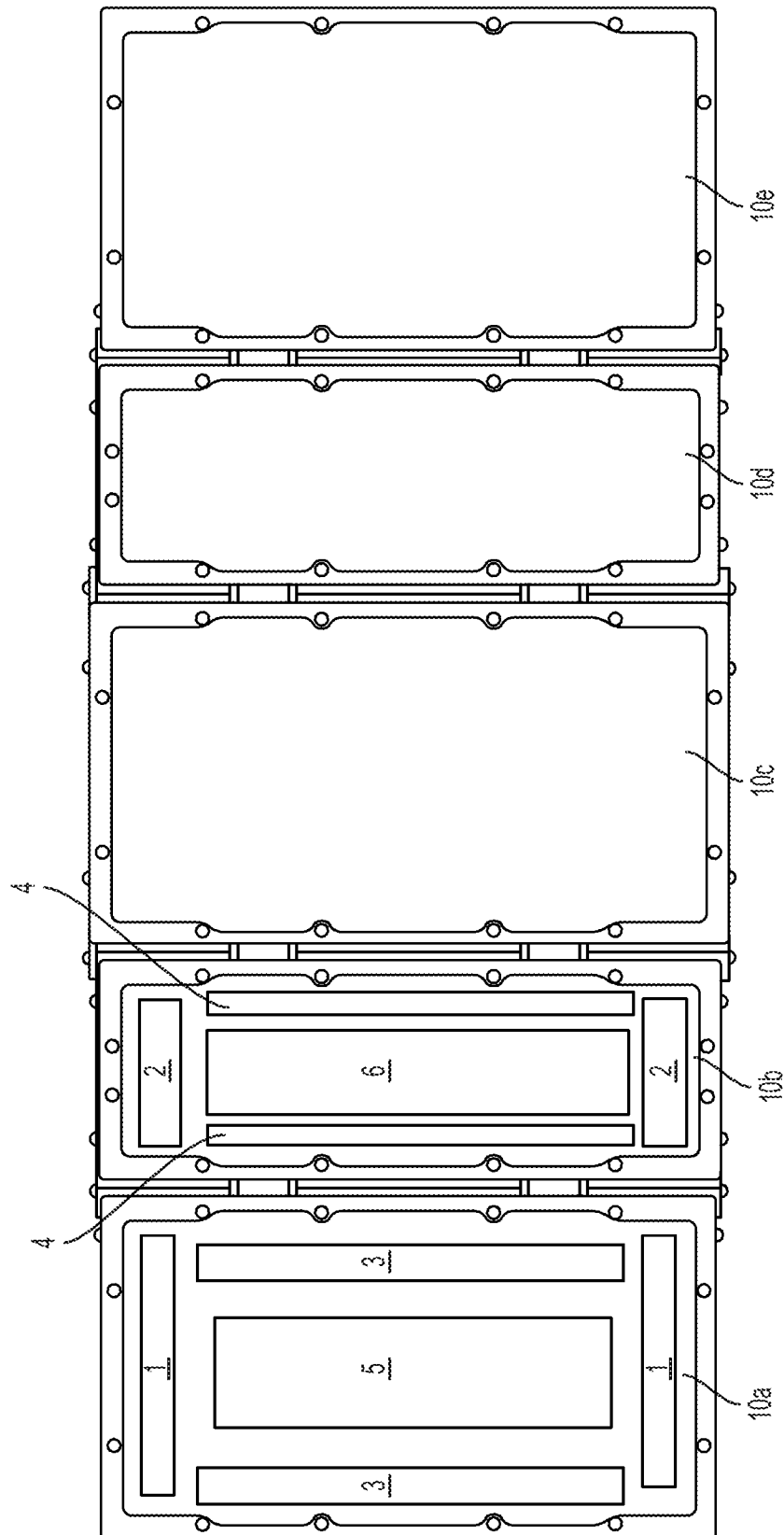


FIG. 5

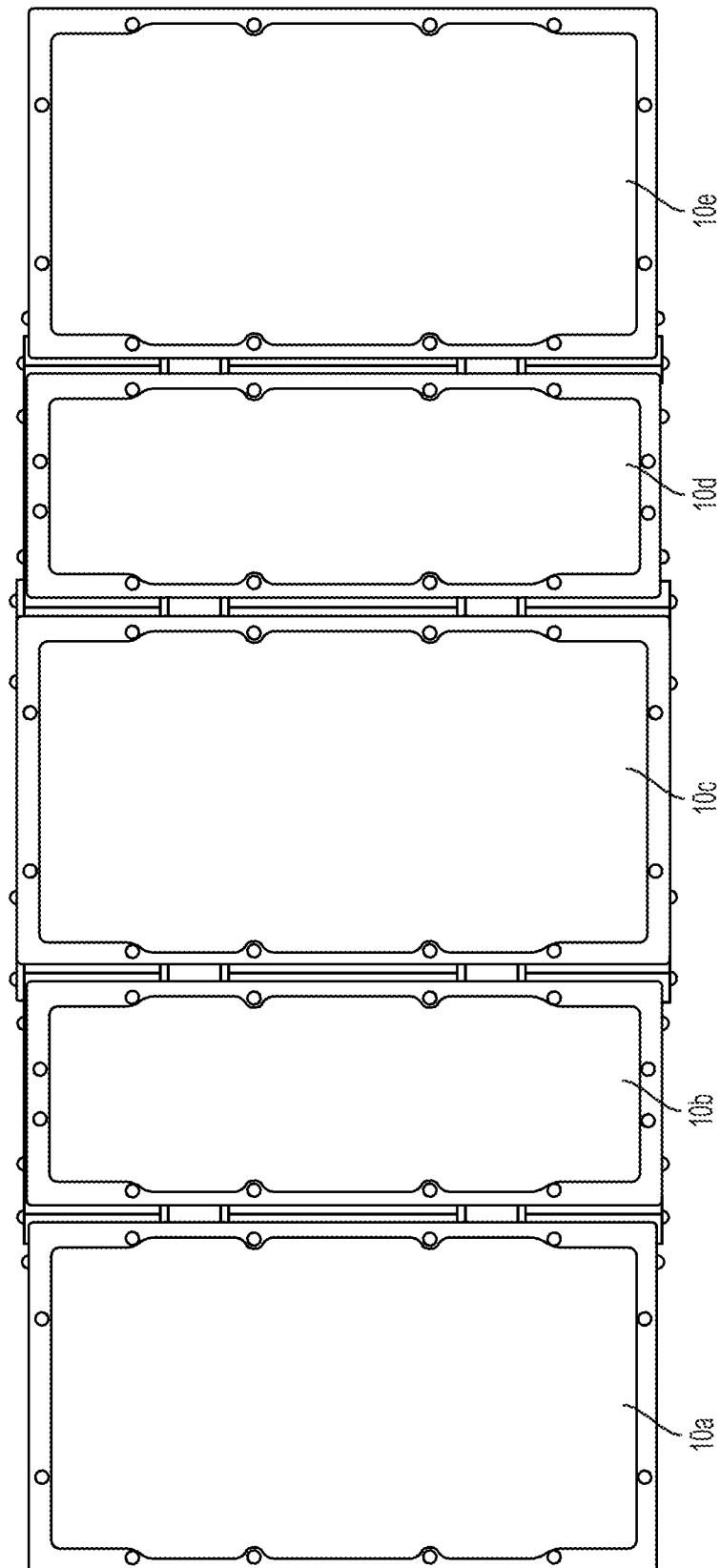


FIG. 6

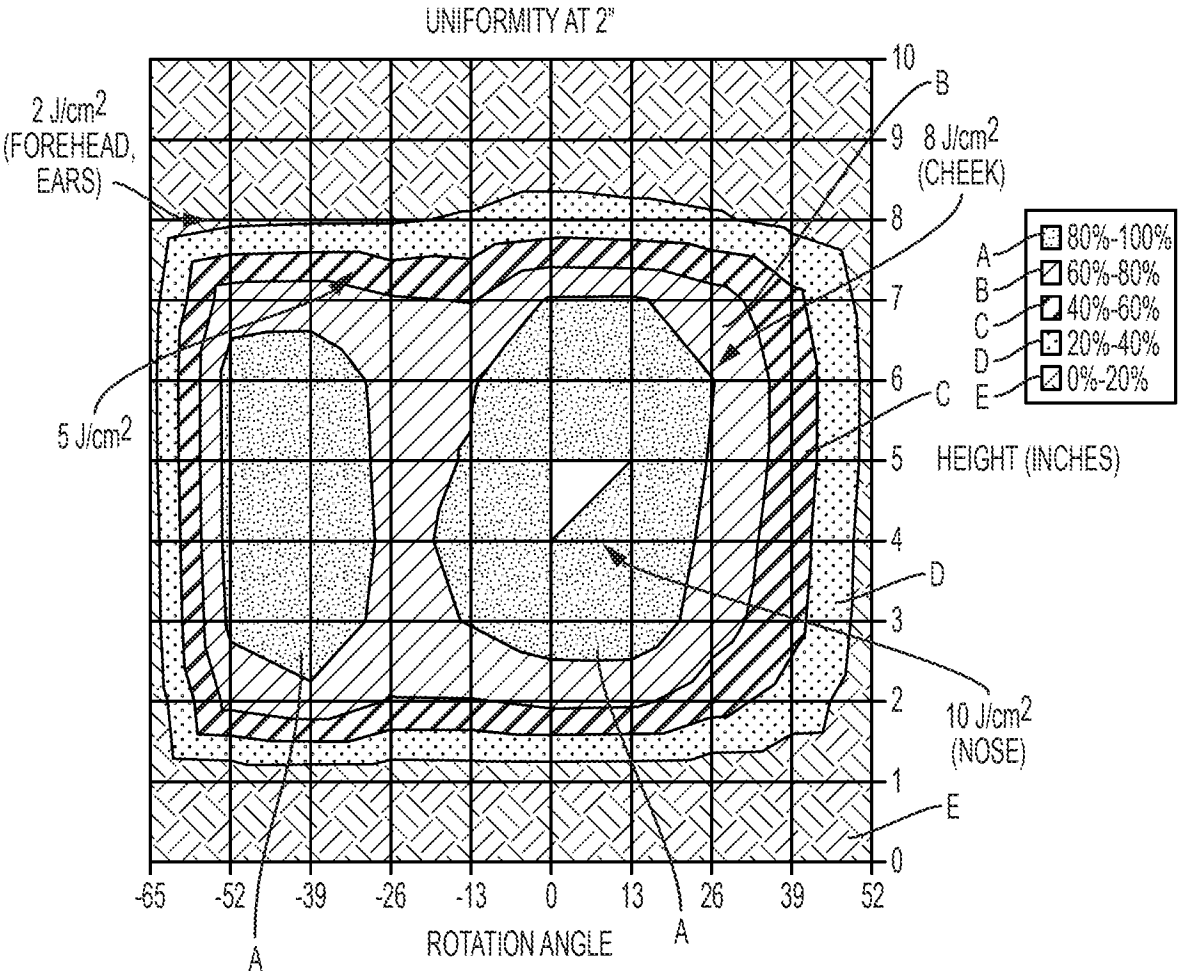


FIG. 7

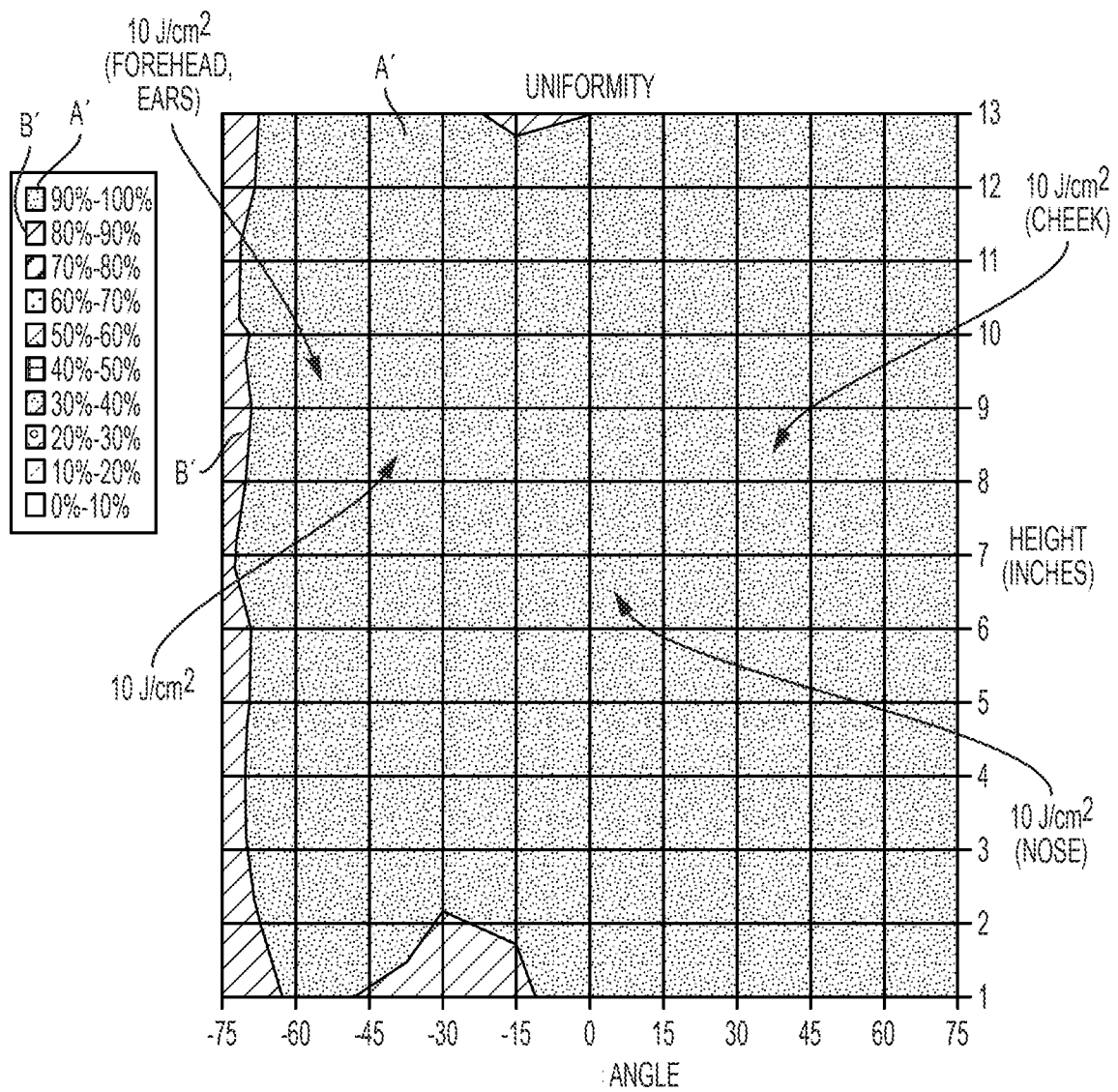


FIG. 8

Electronic Acknowledgement Receipt

EFS ID:	39271245
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	27-APR-2020
Filing Date:	14-FEB-2020
Time Stamp:	14:15:30
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	Applicant Response to Pre-Exam Formalities Notice	ResponseNFCAP.pdf	112810	no	2
			7fc2b6fdc7ee94bd4397a3de20059512c737a6c0		

Warnings:

Information:					
2	Drawings-only black and white line drawings	ReplacementSheets.pdf	1258413	no	8
			90aa51fac6b0d238e9368a14154936141ea5e3e6		
Warnings:					
Information:					
Total Files Size (in bytes):				1371223	
<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>					

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						Application or Docket Number 16/791,004			
APPLICATION AS FILED - PART I									
(Column 1)		(Column 2)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY			
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)		RATE(\$)	FEE(\$)		
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	300		
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A			N/A	660		
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MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00		
			TOTAL			TOTAL	1720		
* If the difference in column 1 is less than zero, enter "0" in column 2.									
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	Independent (37 CFR 1.16(h))	*	Minus ***	=	x =	OR	x =		
	Application Size Fee (37 CFR 1.16(s))					OR			
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			TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE			
(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY	
AMENDMENT B	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)	
	Total (37 CFR 1.16(i))	*	Minus **	=	x =	OR	x =		
	Independent (37 CFR 1.16(h))	*	Minus ***	=	x =	OR	x =		
	Application Size Fee (37 CFR 1.16(s))					OR			
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))					OR			
			TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE			
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CONFIRMATION NO. 2631

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22428
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109



Date Mailed: 04/28/2020

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Mark Carota, Chelmsford, MA;
Brian Mazejka, Salem, NH;

Applicant(s)

DUSA Pharmaceuticals, Inc., Wilmington, MA;

Assignment For Published Patent Application

DUSA Pharmaceuticals, Inc., Wilmington, MA

Power of Attorney: The patent practitioners associated with Customer Number 22428

Domestic Priority data as claimed by applicant

This application is a DIV of 15/292,731 10/13/2016 PAT 10589122
which claims benefit of 62/241,902 10/15/2015

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.

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Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

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: 03/02/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/791,004**

Projected Publication Date: 08/06/2020

Non-Publication Request: No

Early Publication Request: No
Title

ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

Preliminary Class

362

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.

Substitute for form 1449/PTO
**INFORMATION DISCLOSURE
 STATEMENT BY APPLICANT**

Date Submitted: May 7, 2020

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3792
Examiner Name	Unassigned
Attorney Docket Number	067286-0410

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	B1	Letter to UVBiotek, LLC, dated July 28, 2017, Re: K170187, Trade/Device Name: Photodynamic Therapy Device, available at https://www.accessdata.fda.gov/cdrh_docs/pdf17/K170187.pdf (accessed April 30, 2020)	
	B2	Webpage printout, Hill Laboratories Company, "Akalarus Phototherapy Treatment System with Red, Blue and Infrared Wavelengths by Hill Therapeutics," available at https://hilllabs.com/therapeutics/Akalarus-Photo-Therapy-System.php (accessed April 30, 2020)	

Examiner
Signature

Date
Considered

Electronic Acknowledgement Receipt

EFS ID:	39380451
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Kiri Lee Sharon/Effie Hale
Filer Authorized By:	Kiri Lee Sharon
Attorney Docket Number:	067286-0410
Receipt Date:	07-MAY-2020
Filing Date:	14-FEB-2020
Time Stamp:	15:19:35
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	116814	no	2
			e9d35ea99c1fc97b6428897e3f4ed294fe1b ff56		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	107774	no	1
			51b74a012728b41fe7eaff55bc8ac5452e77001c		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NPL_HillLaboratories.pdf	1800588	no	2
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Warnings:					
Information:					
4	Non Patent Literature	NPL_LTRtoUVBiotek.pdf	3881976	no	9
			6268e28802d80d947d27e8ea3f2811135e68dd89		
Warnings:					
Information:					
			Total Files Size (in bytes):	5907152	
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: Unassigned
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a

competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

CONCISE EXPLANATION OF RELEVANCE

The cited documents are in English.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 7, 2020

By /Kiri Lee Sharon/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828



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
16/791,004	02/14/2020	Thomas Boyajian	067286-0410

CONFIRMATION NO. 2631

PUBLICATION NOTICE



OC000000119011340

22428
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Title:ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

Publication No.US-2020-0246630-A1

Publication Date:08/06/2020

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently <http://www.uspto.gov/patft/>.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently <https://portal.uspto.gov/pair/PublicPair>. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Substitute for form 1449/PTO
**INFORMATION DISCLOSURE
 STATEMENT BY APPLICANT**

Date Submitted: November 12, 2020

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3700
Examiner Name	FRISTOE JR, JOHN K
Attorney Docket Number	067286-0410

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)			
	C1	10,357,567-B1	07-23-2019	LUNDAHL ET AL.	
	C2	2004/0010299-A1	01-15-2004	TOLKOFF ET AL.	
	C3	2009/0324727-A1	12-31-2009	FOGUET ROCA	
	C4	2011/0053965-A1	03-03-2011	TRIGIANTE, GIUSEPPE	
	C5	2014/0010761-A1	01-09-2014	PARENT ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

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 ⁶
	C6	USPTO Office Action, 16/438,702 (067286-0405), 10/13/2020, 17 pages	

Examiner
Signature

Date
Considered

Electronic Acknowledgement Receipt

EFS ID:	41103620
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	12-NOV-2020
Filing Date:	14-FEB-2020
Time Stamp:	11:34:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	117338	no	2
			b2ea9a114726c12169782ebbbab51f48df693bd4		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	107085	no	1
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NPL_OA0405.pdf	704968	no	17
			43cc3e7af49cdd046823c863c670ee6e6a0f3f17		
Warnings:					
Information:					
			Total Files Size (in bytes):	929391	
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR
FOR PHOTODYNAMIC
THERAPY AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: FRISTOE JR, JOHN K
Art Unit: 3700
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Mail Stop AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive

any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Listed on the attached Form PTO/SB/08 are documents cited in a PTO Office Action of a co-pending case (serial no. 16/438,702). The relevance of the references can be found in the PTO Office Action of the co-pending case. A copy of the PTO Office Action in the co-pending case is being submitted herewith (document C6).

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date November 12, 2020

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: January 4, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
Sheet 1 of 1		Application Number		16/791,004	
		Filing Date		2/14/2020	
		First Named Inventor		Thomas BOYAJIAN	
		Art Unit		3700	
		Examiner Name		FRISTOE JR, JOHN K	
		Attorney Docket Number		067286-0410	

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)			
	D1	9,227,082-B2	01-05-2016	MCDANIEL, DAVID H.	
	D2	2001/0021812-A1	09-13-2001	LUNDAHL ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			
	D3	17/109,311	12-02-2020	LUNDAHL 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 Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	D4	USPTO Office Action, 17/009,871 (067286-0411), 12/02/2020, 15 pages	

Examiner Signature		Date Considered	
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Electronic Acknowledgement Receipt

EFS ID:	41542892
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	04-JAN-2021
Filing Date:	14-FEB-2020
Time Stamp:	13:44:49
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	Transmittal Letter	IDSTrans.pdf	116528	no	2
			de4090957b214cbf7148bb2036083a202586e59d		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	106889	no	1
			0559a0bd1c0b8f5322910663eb3da1f685fd b8d0		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NPL_OA_0411.pdf	603590	no	15
			2d62cbd7262a16bcf4775d5bf8a85d2555d c0651		
Warnings:					
Information:					
			Total Files Size (in bytes):	827007	
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: Docket Holding
Art Unit: 3600
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents D1 and D2 on the attached Form PTO/SB/08 are documents cited in a PTO Office Action of a co-pending case (serial no. 17/009,871). The relevance of the references can be found in the PTO Office Action of the co-pending case. A copy of the PTO Office Action in the co-pending case is being submitted herewith (document D4).

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date January 4, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
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Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO
**INFORMATION DISCLOSURE
 STATEMENT BY APPLICANT**

Date Submitted: April 1, 2021

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3600
Examiner Name	HOLDING, DOCKET
Attorney Docket Number	067286-0410

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)			
	E1	5,032,400-A	07-16-1991	WIERSUM ET AL.	
	E2	5,601,838-A	02-11-1997	HIND, HARRY	
	E3	5,686,065-A	11-11-1997	HANEY, DAVID N.	
	E4	6,897,238-B2	05-24-2005	ANDERSON, RICHARD ROX	
	E5	2010/0298758-A1	11-25-2010	CHRISTIANSEN ET AL.	
	E6	2011/0020441-A1	01-27-2011	KLAVERNESS ET AL.	
	E7	2011/0293528-A1	12-01-2011	GODAL ET AL.	
	E8	2013/0304019-A1	11-14-2013	COOPER ET AL.	
	E9	2013/0315999-A1	11-28-2013	PAITHANKAR ET AL.	
	E10	2016/0045757-A1	02-18-2016	GROSETH, MORTEN	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	E11	USPTO Notice of Allowance, 16/438,702 (067286-0405), 03/22/2021, 14 pages	
	E12	USPTO Office Action, Serial No. 17/009,871 (067286-0411), 03/23/2021, 9 pages	
	E13	USPTO Office Action, Serial No. 17/109,311 (067286-0419), 3/2/2021, 16 pages	

Examiner
Signature

Date
Considered

Electronic Acknowledgement Receipt

EFS ID:	42344557
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	01-APR-2021
Filing Date:	14-FEB-2020
Time Stamp:	13:30:27
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	117325	no	2
			674d7278f886e55a7aaef2d0d89c6377f070da7e		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	108691	no	1
			12425679159c3816d8c059ef1e2792d60e0268f4		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NPL_NoA_0405.pdf	1390726	no	14
			edb0118f16c152a8df9b6669a3d9e7bd36f63dc3		
Warnings:					
Information:					
4	Non Patent Literature	NPL_FOA_0411.pdf	837294	no	9
			c843800c2aab79843e3443dca1f98a19a81bec96		
Warnings:					
Information:					
5	Non Patent Literature	NPL_OA_0419.pdf	1529109	no	16
			476fd5cfefaf595c5829a745ff9ae471d6ec5cdf		
Warnings:					
Information:					
Total Files Size (in bytes):			3983145		
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR
FOR PHOTODYNAMIC THERAPY
AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: HOLDING, DOCKET
Art Unit: 3600
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents E1-E10 listed on the attached Form PTO/SB/08 are documents cited in PTO actions of co-pending cases (serial nos. 16/438,702 and 17/109,311). The relevance of the references can be found in the PTO actions of the co-pending cases. A copy of the PTO Notice of Allowance (document E11) and Office Action (document E13) is being submitted herewith.

Document E12 listed on the attached Form PTO/SB/08 is a PTO Office Action issued in a co-pending case (serial no. 17/009,871). A copy of the Office Action is being submitted herewith.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date April 1, 2021

By /Glenn Law/

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Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 13, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3600
Examiner Name	CENTRAL, DOCKET		
Attorney Docket Number	067286-0410		
Sheet	1	of	1

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)			
	F1	2008/0188558-A1	08-07-2008	GODAL ET AL.	
	F2	2009/0247932-A1	10-01-2009	BAROLET, DANIEL	
	F3	2011/0224598-A1	09-15-2011	BAROLET, DANIEL	
	F4	2013/0274834-A1	10-17-2013	BAROLET ET AL.	
	F5	2015/0290028-A1	10-15-2015	ISSEROW ET AL.	
	F6	2016/0008623-A1	01-14-2016	JONES ET AL.	
	F7	2020/0261580-A1	08-20-2020	WILLEY, ANDREA	
	F8	2013/0289089-A1	10-31-2013	MORRIS ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	F9	WO-2019/018408-A1	01-24-2019	WILLEY, ANDREA		

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 ⁶
	F10	DANIEL BAROLET ET AL., Radiant Near Infrared Light Emitting Diode Exposure as Skin Preparation to Enhance Photodynamic Therapy Inflammatory Type Acne Treatment Outcome, Lasers in Surgery and Medicine Vol. 42, No.2, February 1, 2010, pages 171-178	
	F11	Extended European Search Report, Application No. 18835929.3, March 12, 2021, 10 pages	
	F12	JOHANNA T.H.M. VAN DEN AKKER ET AL., Effect of Elevating the Skin Temperature During Topical ALA Application on in vitro ALA penetration Through Mouse Skin and in vivo PpIX production in Human Skin, Photochemical and Photobiological Sciences, Royal Society of Chemistry, Cambridge, GB, Vol. 3, No. 3, March 1, 2004, pages 263-267	
	F13	PETRAS JUZENAS ET AL., Uptake of Topically Applied 5-Aminolevulinic Acid and Production of Protoporphyrin IX in Normal Mouse Skin: Dependence on Skin Temperature, Photochemistry and photobiology, Vol. 69, No. 4, April 1, 1999, pages 478-481	
	F14	International Search Report from PCT/US2018/042505, issued October 2, 2018.	

Examiner Signature		Date Considered	
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 26338.105001 WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2018/042505	International filing date (<i>day/month/year</i>) 17 July 2018	(Earliest) Priority Date (<i>day/month/year</i>) 17 July 2017
Applicant WILLEY, ANDREA		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (see Box No. II).

3. ☐ Unity of invention is lacking (see Box No. III).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☐ the text is approved as submitted by the applicant.
☒ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. 1A
☐ as suggested by the applicant.
☒ as selected by this Authority, because the applicant failed to suggest a figure.
☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/042505

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.: 19, 20
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)) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/042505

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention is directed to methods of treating diseases and disorders of the skin (e.g., acne) with heat-enabled photodynamic therapy (HEPT). Methods of treating acne, non-melanoma skin cancer (NMSC), actinic keratosis (AK) or disseminated superficial actinic porokeratosis (DSAP) using red light photodynamic therapy on heat-treated skin.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2018/042505

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 41/00; A61N 5/062; A61P 17/10 (2018.01)

CPC - A61K 9/0014; A61K 41/0057; A61K 41/0061; A61N 5/0616; A61N 5/062; A61N 2005/0643; A61N 2005/065; A61P 17/10 (2018.08)

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)

See Search History document

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

USPC - 514/410; 604/20; 607/88 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/0247932 A1 (BAROLET) 01 October 2009 (01.10.2009) entire document	1-4, 7, 12, 13, 16-18, 21-23, 26, 27

Y		5, 6, 8-11, 14, 15, 24, 25
Y	US 2015/0290028 A1 (ISSEROW et al) 15 October 2015 (15.10.2015) entire document	5
Y	US 2013/0274834 A1 (BAROLET et al) 17 October 2013 (17.10.2013) entire document	6, 24, 25
Y	US 2016/0008623 A1 (PHOTOCURE ASA) 14 January 2016 (14.01.2016) entire document	8, 10, 11, 14, 15
Y	US 2009/0324727 A1 (FOGUET ROCA) 31 December 2009 (31.12.2009) entire document	9
A	US 2015/0238776 A1 (THE GENERAL HOSPITAL CORPORATION D/B/A MASSACHUSETTS GENERAL HOSPITAL) 27 August 2015 (27.08.2015) entire document	1-18, 21-27
A	US 2013/0289089 A1 (MORRIS et al) 31 October 2013 (31.10.2013) entire document	1-18, 21-27
A	US 2008/0188558 A1 (GODAL et al) 07 August 2008 (07.08.2008) entire document	1-18, 21-27

☐ 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 August 2018

Date of mailing of the international search report

02 OCT 2018

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, VA 22313-1450
Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)



- (51) International Patent Classification:
A61K 41/00 (2006.01) *A61P 17/10* (2006.01)
- (21) International Application Number:
PCT/US2018/042505
- (22) International Filing Date:
17 July 2018 (17.07.2018)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
62/533,558 17 July 2017 (17.07.2017) US
62/534,973 20 July 2017 (20.07.2017) US
- (72) Inventor; and
- (71) Applicant: **WILLEY, Andrea** [US/US]; 2277 Fair Oaks
Boulevard, Sacramento, CA 95825 (US).
- (74) Agent: **KAUFMAN, Rebecca**; King & Spalding, 1180
Peachtree Street, Atlanta, GA 30309 (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, DJ, DK, DM, DO,

DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,
KR, KW, 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.

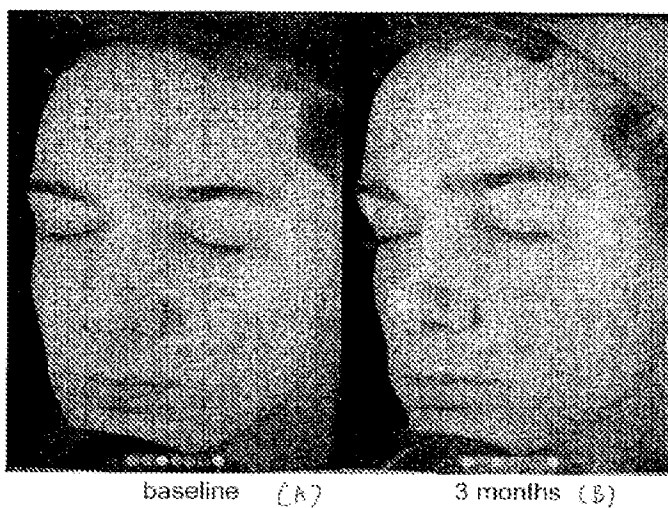
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, 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: PHOTODYNAMIC THERAPY METHOD FOR SKIN DISORDERS

Fig. 1

Inflammatory and cystic Acne:
1 hour 10% ALA gel 40C 37J/cm² 630nm red light



clear 3
months after
single
treatment

(still clear
6 months)

(57) Abstract: The present invention is directed to methods of treating diseases and disorders of the skin (e.g., acne) with heat-enabled photodynamic therapy (HEPT). Methods of treating acne, non-melanoma skin cancer (NMSC), actinic keratosis (AK) or disseminated superficial actinic porokeratosis (DSAP) using red light photodynamic therapy on heat-treated skin.

PHOTODYNAMIC THERAPY METHOD FOR SKIN DISORDERS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Patent Application 62/533,558, filed July 17, 2017 and U.S. Provisional Patent Application 62/534,973, filed July 20, 2017, the contents of which are herein incorporated by reference in their entirety.

FIELD OF THE INVENTION

The present invention relates generally to methods of treating diseases and disorders of the skin using red light photodynamic therapy in conjunction with heating. In particular embodiments, the present invention relates to methods of treating acne, non-melanoma skin cancer (NMSC), actinic keratosis (AK) or disseminated superficial actinic porokeratosis (DSAP) using red light photodynamic therapy on heat-treated skin.

BACKGROUND OF THE INVENTION

Skin disease is among the most common human illnesses, affecting between 30% and 70% of the population, with even higher rates in at-risk subpopulations. (Hay RJ et al., *J Invest Dermatol.* 2014; 134(6): 1527-1534). The healthcare burden is equally significant, estimated at nearly \$27 direct health care costs and an addition 11 billion in lost productivity. (Lim HW et al. *J Am Acad Dermatol.* 2017; 76: 958-972).

Acne is the most common skin disease. Non-inflammatory acne is the most common type, characterized by whiteheads and blackheads. Inflammatory acne typically involves a bacterial (*P. acnes*) infection and is characterized by papules, pustules, nodules, and cysts. The most common trigger for both types of acne is hormonal, with most individuals experiencing at least a mild form of acne in adolescence. Other triggers may include diet, stress and certain medications. Because acne affects the appearance, and often at a critical age, it can negatively impact the quality of life. (Kligman AM. *J Invest Dermatol.* 1974;62:268-87).

Various methods for treating acne are known, including topical agents such as benzoyl peroxide, retinoids and antibiotics. (Thiboutot D, et al. *J Am Acad Dermatol.* 2009;60(Suppl 5):S1-50). Systemic agents may be used as well, including antibiotics, retinoids and hormone

therapy. Yet, many of these approaches have undesirable side effects and/or fail to produce an acceptable result. Antibiotic resistance is increasing, with many countries reporting that more than 50% of *P. acnes* strains are resistant to particular topical agents.

Ultraviolet (UV)/blue light is approved by the FDA for the treatment of mild to moderate acne, due to its anti-inflammatory effects mediated on skin cells. A procedure combining a photosensitive agent and high intensity red light has been demonstrated to be effective, but with significant side effects. (Hongcharu W, et al., *J Invest Dermatol.* 2000 Aug;115(2):183-92), Sakamoto FH et al., *J Am Acad Dermatol.* 2010 Aug;63(2):183-93), (Sakamoto FH et al. *J Am Acad Dermatol.* 2010 Aug;63(2):195-211). As a result, this approach has been reserved for the most serious cases of acne.

There remains a need for novel approaches to treatment of skin diseases and disorders, including acne but not limited to acne, which provide improved results and limits side effects.

SUMMARY OF THE INVENTION

The present invention provides a method of treating skin diseases or disorders using red light photodynamic therapy on pre-heated skin.

In embodiment first aspect, the present invention is a method of treating facial acne in a subject in need thereof, comprising (i) applying heat to an affected area of the subject's skin using a thermal delivery device to achieve a skin temperature of between about 38 and about 42°C for a suitable time; (ii) incubating a pharmaceutical composition comprising a photoactive agent for a period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) applying a therapeutically effective amount of the incubated pharmaceutical composition to the affected area; (iv) administering a suitable dose of red light to the affected area, therapy treating the facial acne.

In one embodiment, the acne is mild acne, moderate acne or severe acne.

In another embodiment, the acne is comedonal, papulopustular or nodulocystic.

In one embodiment, the thermal delivery device is a heat mask. In a particular embodiment, the thermal delivery device is an acetate mask that heats upon crystallization.

In one embodiment, the affected area is heated for about 60 minutes.

In a particular embodiment, the affected area is heated to about 40°C.

In a particular embodiment, the incubation period is less than about 14 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 14 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 3 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 3 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 1 hour but achieves the same effect as if the pharmaceutical composition was incubated for about 1 hour in the absence of step (i).

In an exemplary embodiment, the incubation period is less than about 10, less than about 5 or less than about 1 minute.

In one embodiment, the pharmaceutical composition is a nanoemulsion comprising 10% 5-aminolevulinic acid HCl.

In another embodiment, the light has a wavelength of between about 620 to about 640 nm, and more particularly, about 630 nm.

In one embodiment, the suitable dose of light is about 37 J/cm².

In exemplary embodiments, the treatment results in a reduction in the subject's acne lesion count. In a particular embodiment, the reduction persists for a period of at least three months.

In exemplary embodiments, treatment results in a reduction in the subject's acne lesion severity. In a particular embodiment, the reduction persists for a period of at least three months.

In exemplary embodiments, the side effects of treatment are reduced relative to a method that does not include step (i).

In a second aspect, the present invention is a method of treating non-melanoma skin cancers of the face in a subject in need thereof, comprising (i) applying heat to an affected area of the subject's skin using a thermal delivery device to achieve a skin temperature of between about 38 and about 42°C for a suitable time; (ii) incubating a pharmaceutical composition comprising a photoactive agent for a period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) applying a therapeutically effective amount of the incubated

pharmaceutical composition to the affected area; (iv) administering a suitable dose of red light to the affected area, therapy treating the non-melanoma skin cancer of the face.

In a particular embodiment, the non-melanoma skin cancer is basal cell carcinoma (BCC). The BCC may be primary, recurrent or incompletely excised previously.

In another particular embodiment, the non-melanoma skin cancer is a squamous cell carcinoma (SCC). The SCC may be primary, recurrent or incompletely excised previously.

In one embodiment, the non-melanoma skin cancer is a basal cell carcinoma and heat is applied in (i) for about thirty minutes.

In another embodiment, the non-melanoma skin cancer is basal cell carcinoma and heat is applied in (i) for about twenty minutes.

In exemplary embodiments, the side effects of treatment are reduced relative to method that do not include step (i).

In a particular embodiment, the incubation period is less than about 14 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 14 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 3 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 3 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 1 hour but achieves the same effect as if the pharmaceutical composition was incubated for about 1 hour in the absence of step (i).

In an exemplary embodiment, the incubation period is less than about 10, less than about 5 or less than about 1 minute.

In a third aspect, the present invention is a method of treating actinic keratosis (AK) of the face in a subject in need thereof, comprising (i) applying heat to an affected area of the subject's skin using a thermal delivery device to achieve a skin temperature of between about 38 and about 42°C for a suitable time; (ii) incubating a pharmaceutical composition comprising a photoactive agent for a period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) applying a therapeutically effective amount of the incubated

pharmaceutical composition to the affected area; (iv) administering a suitable dose of red light to the affected area, therapy treating the actinic keratosis.

In one embodiment, the affected area is heated for about 30 minutes.

In a particular embodiment, the affected area is heated to about 40°C.

In exemplary embodiments, the side effects of treatment are reduced relative to method that do not include step (i).

In a particular embodiment, the incubation period is less than about 14 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 14 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 3 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 3 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 1 hour but achieves the same effect as if the pharmaceutical composition was incubated for about 1 hour in the absence of step (i).

In an exemplary embodiment, the incubation period is less than about 10, less than about 5 or less than about 1 minute.

In a fourth aspect, the present invention is a method of treating disseminated superficial actinic porokeratosis (DSAP) of the face in a subject in need thereof, comprising) applying heat to an affected area of the subject's skin using a thermal delivery device to achieve a skin temperature of between about 38 and about 42°C for a suitable time; (ii) incubating a pharmaceutical composition comprising a photoactive agent for a period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) applying a therapeutically effective amount of the incubated pharmaceutical composition to the affected area; (iii) administering a suitable dose of red light to the affected area, therapy treating the DSAP.

In exemplary embodiments, the side effects of treatment are reduced relative to method that do not include step (i).

In a particular embodiment, the incubation period is less than about 14 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 14 hours in the

absence of step (i).

In a particular embodiment, the incubation period is less than about 3 hours but achieves the same effect as if the pharmaceutical composition was incubated for about 3 hours in the absence of step (i).

In a particular embodiment, the incubation period is less than about 1 hour but achieves the same effect as if the pharmaceutical composition was incubated for about 1 hour in the absence of step (i).

In an exemplary embodiment, the incubation period is less than about 10, less than about 5 or less than about 1 minute.

BRIEF DESCRIPTION OF THE FIGURES

FIGURE 1: shows the results of treating inflammatory and cystic acne with the method of the present invention described in Example 1. As indicated in the figure, the subject remains clear for three months (Figure 1B) and at least six months.

FIGURE 2: shows the results of treating inflammatory and cystic acne with the method of the present invention as described in Example 1 at different time intervals and using a porphyrin camera (Figure 2B).

FIGURE 3: shows the results of treating nodular basal cell carcinoma on the extremities according to the method of the present invention described in Example 2. A wide margin of porphyrins is shown in the heated area in Figure 3B using a porphyrin camera.

FIGURE 4: shows the results of recurrent nodular and infiltrative basal cell carcinoma on the extremities according to the method of the present invention described in Example 3.

FIGURE 5: shows the results of treating infiltrating basal cell carcinoma of the skull according to the method of the present invention described in Example 4.

FIGURE 6: shows the results of treating infiltrating basal cell carcinoma of the skull according to the method of the present invention described in Example 5, including histology at baseline (Figure 6A) and one (1) month post treatment (Figure 6B), showing no residual BCC.

FIGURE 7: shows the results of treating SCC-IS according to the method of the present invention described in Example 5. Heat is shown to create an increased porphyrin margin around the affected area, reflecting an increase in absorption.

FIGURE 8: shows the results of treating multi-focal basal cell carcinoma using the method of the present invention.

FIGURE 9: shows the results of treating refractory disseminated porokeratosis with related SCC using the method of the present invention described in Example 6.

FIGURE 10: shows the results of treatment as described in Example 7, including significant production of porphyrins after 20 minutes of incubation of the 20% ALA gel.

FIGURE 11: shows the results of treatment as described in Example 8, including even greater production of porphyrins after 30 minutes of incubation of the 20 % ALA gel.

FIGURE 12: shows the results of treatment as described in Example 9, in the absence of heat, showing minimal production of porphyrins after 60 minutes incubation of the 20% ALA gel.

FIGURE 13: shows porphyrin images during simultaneous incubation of a 20% ALA solution.

FIGURE 14: shows images of treatment without heat (Figure 14A) or with heat (Figure 14B) using a 20% ALA solution, evidenced increased PDT reaction immediately post PDT on the heated side (Figure 14C).

FIGURE 15: shows the various settings utilized for the heating pad at one (1) minute and when measured between about 15 and about 60 minutes.

FIGURE 16: shows the results of the method of the present invention employing a seventeen (17) minute incubation of a 20% ALA solution and utilizing a space heater with a temperature of between about 38°C and about 42°C.

FIGURE 17: shows the results of the method of the present invention employing a one hour incubation with 10% aminolevulinic acid (ALA) with a sodium acetate warming mask (skin temperature 40C) followed by 37J/cm² 635nm red light when treating an index patient with moderate inflammatory and pustular acne on the face. The reduction in lesion counts was persistent 9 months after a single thermal PDT, as detailed in Example 10.

FIGURE 18: shows the results of the method of the present invention employing a one hour incubation with 10% aminolevulinic acid with a sodium acetate warming mask (skin temperature 40C) followed by 37J/cm² 635nm red light when treating an index

patient with moderate inflammatory and pustular acne on the face. Remodeling of acne scars is shown 9 months after single thermal PDT, as detailed in Example 11.

FIGURE 19: shows the margin of porphyrins created around a basal cell carcinoma (BCC) on the forearm greater than ten times the size of the original lesion following one hour incubation with ALA 20% under a heating pad set at medium (skin temperature 39°C). The area of the BCC is 3,580² and the area of the BCC and porphyrins is 36,082².

FIGURE 20: shows the margin of porphyrins created around a squamous cell carcinoma (SCC) on the foot nine times the size of the original lesion following 30 minute incubation with ALA 20% under a sodium acetate warming pouch (skin temperature 42°C). The area of the SCC is 1,051² and the area of the SCC and porphyrins is 9,269².

FIGURE 21: shows clearance of basal cell carcinoma (BCC) on the chest 2 months following 30 minute incubation with ALA 10% under a sodium acetate warming pouch (skin temperature 42°C) with margin of porphyrins demonstrated with porphyrin imaging.

FIGURE 22: shows the results of a split-face study with porphyrin imaging demonstrating the increase in porphyrin production on facial skin following incubation with 10% aminolevulinic acid (ALA) for 30 minutes with skin temperature at 40°C (using a sodium acetate warming mask) compared to standard 3 hour incubation at room temperature (skin temperature at 30°C).

FIGURE 23: shows the increased porphyrin production on facial skin with actinic keratoses following 30 minute incubation with 20% ALA at 40C using a sodium acetate warming mask compared to the standard one hour incubation at room temperature (room temperature 70°F, skin temperature 30°C). Increased porphyrin production was determined and shown as described in Example 12.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the observation that heating of the skin increases the efficacy of photodynamic therapy (PDT), permitting a reduction in incubation time for the photosensitive agent (or pharmaceutical composition comprising the same) as well as increased absorption of the photoactive agent (or pharmaceutical composition comprising the same). In

exemplary embodiments, the method of the present invention permits improved results, including complete clearance and/or reduced recurrence of the disease or disorder.

I. Definitions

The term “acne” as used herein refers to inflammatory diseases of the pilosebaceous follicles and/or skin glands, and commonly is characterized by papules, pustules, cysts, nodules, comedones, other blemishes or skin lesions.

The term “actinic keratosis” or “AK” as used herein refers to precancerous skin lesions caused by and associated with chronic exposure to radiant energy, such as sunlight. Actinic keratosis lesions are small, red, rough hyperkeratotic lesions occurring on sun exposed areas of the skin.

The term “administer” and “administration” as used herein refers to providing or causing the provision of a material to a subject, such as by a topical, subdermal, subcutaneous, intradermal, enteral, parenteral, rectal, nasal, intravenous, intramuscularly, intraperitoneal, or other route.

The term “basal cell carcinoma” or “BCC” as used herein refers to a malignant neoplasm of the keratinocytes that reside in the basal layer of the epidermis. It commonly develops on areas exposed to UV rays, particularly the head, face and neck. Although BCC does not typically spread beyond the primary site, it can be locally destructive. BCC may be classified as nodular ulcerative, superficial, pigmented or morpheaform.

The term “blue light” as used herein refers to light having a wavelength between about 380 nm and 500 nm, with visible blue light having a wavelength of about 475 nm.

The term “cancer” as used herein refers to a disease or disorder characterized by uncontrolled cell division and in many instances the ability of these cells to invade other tissues by the direct growth in adjacent tissue through invasion or by the implantation in distant sites through metastasis.

The term “drug- to-light interval” as used herein refers to the period of time between the administration of photosensitizing agent to the affected area and the administration of light to the affected area.

The term “duration of exposure” as used herein refers to the amount of time that skin is

continuously exposed to a therapeutic agent (e.g., drug) or other therapeutic modality (e.g., heat, light).

The term "duration of treatment" as used herein refers to the amount of time between the initiation and completion of one cycle of treatment.

The term "effective amount" as used herein refers to an amount that elicits the biological or medicinal response in a tissue, system, animal, or human that is being sought, either alone or as a component of a therapeutic regime.

The term "'essentially no" as used herein in the context of tolerability refers to insignificant or *de minimis* occurrences of skin irritation events manifested in symptoms such as burning or stinging, flushing or blushing, or mild transient events.

The term "essentially no" as used herein in the context of safety refers to insignificant or *de Minimis* occurrences of systemic or serious adverse events.

The term "heat- to-drug interval" as used herein refers to the period of time between the administration of heat to the affected area and the administration of the photosensitizing agent to the affected area.

The terms "high rates of clinical response" or "high efficacy" or "substantial decrease" in the context herein can relate to a reduction of about 45% or more in lesion count or to where subjects met a success criterion of "clear" or "almost clear" or to an "improvement of 2 grades from the baseline".

The term "high risk location" as used herein with reference to a non-melanoma skin cancer refers to areas of the face including the central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermillion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear); genitalia; hands, and feet.

The term "inhibiting" (and similar terms such as or "reducing" "lessening" or "preventing" or "avoiding" or any variation of these terms) as used herein refers to any measurable decrease or complete inhibition to achieve a desired result.

The term "lesion" as used herein refers to a diseased area of skin.

The term "lesion count" as used herein refers to the number of lesions (e.g., papules and pustules) present in a designated area of the body (e.g., in case of face, on the forehead, left and

right cheeks, nose and chin).

The term "light" or "radiation" or similar terms as used herein includes all wavelengths. Preferably, the radiation wavelength is selected to match the wavelength(s) which excite(s) the photosensitizing agent. Even more preferably, the radiation wavelength matches the excitation wavelength of the photosensitive compound and has low absorption by the non-target tissues. The radiation is further defined in this invention by its intensity, duration, and timing with respect to dosing with the photosensitive agent. The intensity must be sufficient for the radiation to penetrate skin and/or to reach the target tissues to be treated. The duration must be sufficient to photoactivate enough photosensitive agent to act on the target tissues.

The term "low dose light" refers to a dosage of light, at a wavelength capable of being absorbed by the photosensitizer, that does not cause evident cell damage, necrosis, erythema or inflammation.

The term "low risk location" as used herein with reference to a non-melanoma skin cancer refers to areas of the trunk or extremities.

The term "margin" as used herein refers to the area immediately adjacent to, or surrounding, a tumor site but not showing any visible signs of carcinoma. The recommended "standard" surgical margins for various malignant lesions of skin are different.

The term "moderate risk location" as used herein with reference to non-melanoma skin cancer includes the cheeks, forehead, scalp, and neck.

The term "photodynamic therapy" or "PDT" as used herein refers to a technique involving the administration of administration of photosensitizing agents (e.g., to the skin or mucosa) followed by exposure to photoactivating light in order to activate the photosensitizing agents and convert them into cytotoxic form resulting in the destruction of cells and thus treatment of the disease. (See Kennedy JC. et al. *J Photochem Photobiol B*. 1990).

The terms "photosensitizing agent" or "photosensitizer" "or photoactive" are the like are used herein refers to a material, element, chemical, solution, compound, matter, or substance which is sensitive, reactive, receptive, or responsive to light energy. In certain embodiments, the photosensitizing agent may be activatable, i.e., controlled single O₂ production that responds specifically to certain biomarkers.

The term "porphyrin" as used herein refers to a group of heterocyclic macrocycle organic

compounds, composed of four modified pyrrole subunits interconnected at their α carbon atoms via methine bridges ($=CH-$). Expanded porphyrins result from the expansion of the π electron conjugation by increasing the number of heterocyclic rings or bridging carbons of the existing porphyrin framework.

The term “red light” as used herein refers to light having a wavelength of between about 620 nm and about 750 nm.

The term “safe” as used herein means having no or essentially no adverse events (e.g., any unfavorable or unintended sign, symptom, or disease that appears or worsens on the course of treatment).

The term “scar” as used herein refers to marks created during the healing of damage to the skin or tissues. A scar is permanent and cannot be completely removed. Scars treated according to the method described herein include, for example, atrophic scar and hypertrophic scar. More particularly, the acne scar may be an ice pick, boxcar, rolling, bridges and tunnels, gross atrophy, dystrophic or keloid scars.

The term “target” as used herein refers to cells or tissue of the subject that is intended to be impaired or destroyed by the disclosed method. The target takes up the photosensitizing agent; then when sufficient radiation is applied, the target tissue is impaired or destroyed. Conversely, the term “non-target” as used herein refers to cells or tissue of the subject which are not intended to be impaired or destroyed by the treatment method. These non-target cells include but are not limited to those of other healthy tissues.

The term “therapeutically effective amount” as used herein refers to the amount of a therapeutic agent or modality that is sufficient to treat a subject. Effective amounts of the therapeutic agent and/or modality will vary according to factors such as the degree of susceptibility of the individual, the age, gender, and weight of the individual and idiosyncratic responses of the individual.

The term “topical” as used herein refers to directly laying on or spreading on the skin in need of the treatment, e.g., by use of the hands or an applicator.

The term “skin” as used herein refers to the multilayer organ including the epidermis, dermis, and hypodermis (i.e., subcutaneous tissue) that covers the majority of the surface of mammalian subjects such as human beings, and also includes mucous membranes that are

contiguous with the outer skin.

The term “skin cancer” as used herein refers to lentigo, maligna, melanoma, keratoacanthoma, basal cell carcinoma (BCC), squamous cell carcinoma (SCC), Merkel cell carcinoma (MCC), sarcoma, angiosarcoma, cutaneous lymphoma, sweat gland carcinoma and sebaceous gland carcinoma.

The term “squamous cell carcinoma” or “SCC” as used herein refers to a form of skin cancer that develops in the squamous cells of the skin, sometimes referred to as cutaneous squamous cell carcinoma. Similar to BCC, SCC tends to affect areas of skin with high levels of UV exposure such as the head, face and neck. SCCs are usually fast-growing and prone to metastasize. It may arise *de novo* or from actinic keratosis (approximately 0.5 to 16% conversion rate). It is generally classified as SCC *in situ* (involving the full thickness of the epidermis) or invasive (penetrating the basal membrane). Invasive SCC can be further classified as well, moderately or poorly differentiated.

The term “subject” as used herein refers to mammals, e.g., humans, companion animals (e.g., dogs, cats, birds, and the like), farm animals (e.g., cows, sheep, pigs, horses, fowl, and the like) and laboratory animals (e.g., rats, mice, guinea pigs, birds, and the like). In some embodiments, the subject is human.

The term “thermal treatment device” as used herein refers to any device that is capable of heating the skin, whether directly or indirectly.

The term “treat” or “treating” as used herein refers to (i) preventing or delaying the appearance of clinical symptoms of the disease developing in a mammal; (ii) inhibiting the disease i.e. arresting, reducing or delaying the development of the disease or a relapse thereof or
at least one clinical or subclinical symptom thereof, or (iii) relieving or attenuating one or more of the clinical or subclinical symptoms of the disease.

The term “topical” as used herein relates to the administration of a compound by means of the application on the body surface and includes but is not limited to transdermal administration and administration through the mucous membrane.

II. Methods of Treatment

The present invention provides methods of treating disease or disorder of the skin using photodynamic therapy (PDT) in combination with heat.

Advantageously, the method of the present invention permits a reduction in incubation time for the photosensitive agent and/or duration of treatment compared to methods known in the art while achieving equivalent or superior results. In exemplary embodiments, the method of the present invention provides improved results relative to conventional treatments. When used to treat skin cancer, it permits an increase in complete incision rates resulting a reduction in recurrence or time to recurrence.

In one embodiment, present invention is a method of treating a skin disease or disorder in a subject in need thereof, comprising (i) administering heat to an affected area of the subject's skin using a thermal delivery device to achieve suitable temperature for a suitable time; (ii) incubating a pharmaceutical composition comprising a photoactive agent for a period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) administering a therapeutically effective dose of the incubated pharmaceutical composition to the affected area for a suitable time period; (iii) administering a dose of light to the affected area, thereby treating the skin disease or disorder.

Skin Diseases and Disorders

The disease or disorder of the skin treated by the method of the present invention may vary. In a particular embodiment, the skin disease or disorder is a cancerous lesion, pre-cancerous lesion or acne. Areas of skin that can be treated include portions of skin on the head, face, neck, arms, legs, and torso, hands, and feet. In a particular embodiment, the area to be treated is the head face, neck or portions thereof.

Actinic keratosis. In one embodiment, the skin disorder treated according to the method of the present invention is a pre-cancerous lesion. In a particular embodiment, the pre-cancerous lesion is actinic keratosis (AK). AK (also known as solar keratosis) is the most common precancerous skin lesion, appearing as a crusty, scaly growth that often occurs in multiples. Actinic keratosis lesions generally measure in size between about 2 to about 7 millimeters in diameter. AK lesions can range in color from skin-toned to reddish and is often hyperkeratotic.

AK is typically caused by overexposure to ultra violet (UV) light. In rare instances, AK may be caused by overexposure to x-rays. These lesions typically appear on sun-exposed areas

including the face, head (bald scalp), ears, shoulders, neck, arms, forearms and hands. In a particular embodiment, the disease or disorder treated according to the method of the present invention is AK on the face, neck or a portion thereof.

In one embodiment, the method of the present invention is used to treat a pre-cancerous lesion other than actinic keratosis. In a particular embodiment, the method of the present invention is used to treat a disease or disorder of the skin other than actinic keratosis.

Non-melanoma skin cancer. In another embodiment, the skin disorder treated according to method of the present invention is a cancerous lesion. In a particular embodiment, the cancerous lesion is a non-melanoma skin cancer (NMSC). Non-melanoma skin cancer includes all the types of cancer that occur in the skin that are not melanoma. The most common types of NMSC are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). BCC and SCC are also sometimes referred to as "keratinocyte carcinomas" to distinguish them from melanoma.

Basal cell carcinoma arises from basal keratinocytes of the epidermis, hair follicles, and eccrine sweat ducts. About 80% of skin cancers develop from this type of cell, typically on the head and neck (about 90%). BCC usually grows slowly (e.g., 1-2 cm over several years) and rarely spreads to other parts of the body (0.0003-0.05%). The tumor infiltrates tissues in a three-dimensional fashion through the irregular growth of subclinical finger-like outgrowths which remain contiguous with the main tumor mass. The actively growing tissue is at the periphery of the lesion, with cellular apoptosis and resultant ulceration in the central region.

The clinical features of BCC depend upon the subtype. Nodular BCC (also known as "classic basal-cell carcinoma") is the commonest subtype (greater than 60% of cases), and presents as pink nodules, with rolled edges, surface telangiectasia and ulceration or crusting.

Superficial BCCs account for up to 20% of cases and are found often on the trunk over sun-protected sites. Appearing as pink scaly macules or thin plaques, they may be mistaken for Bowen's disease, psoriasis, discoid eczema or tinea corporis. Pigmented BCC occurs more commonly in patients from the Far East and may be mistaken for nodular melanoma. Morphoeic (sclerosing) BCC (also known as Cicatricial basal-cell carcinoma) has the worst prognosis and appears as subtle scar-like plaques, with ill-defined margin.

Histologically, BCC may be undifferentiated or differentiated. Undifferentiated BCC typically includes pigmented BCC, superficial BCC, sclerosing BCC and infiltrative BCC (a

histologic subtype). Nodular BCC is typically differentiated. Other forms of differentiated BCC include keratotic BCC, BCC with sebaceous differentiation and adenoid BCC. Types of biopsy that may be used to confirm the diagnosis and determine the histologic subtype of BCC include shave biopsy and punch biopsy.

In one embodiment, the method of the present invention is used to treat undifferentiated BCC, and more particularly, superficial BCC.

In another embodiment, the method of the present invention is used to treat differentiated BCC, and more particularly, nodular BCC.

In exemplary embodiments, the BCC treated according to the method of the present invention has a mixed histological pattern, i.e., contains two or more major histologic patterns.

BCC is mainly caused by cumulative exposure to UV light, but can occur in subjects who have previously received radiation. Older age and male gender are associated with increased risk. Other risk factors include burn scars, small pox scars, xeroderma pigmentosa and basal cell nevus syndrome. Following development of a BCC, patients are at significantly increased risk of developing subsequent BCCs at other site.

In one embodiment, the method of the present invention may be used to treat BCC. In a particular embodiment, the method may be used to treat BCC selected from the group consisting of nodular, micronodular, cystic, infiltrative, superficial, pigmented, Rodent ulcer (also known as a "Jacobi ulcer"), fibroepithelioma of Pinkus, polyploid, pore-like or aberrant BCC.

In exemplary embodiments, the BCC treated according to the present invention is present on the head, neck or face. In one embodiment, the BCC is present at a target site selected from the nose, cheek, periorbital area, auricular area, ear, temple, forehead or scalp.

In exemplary embodiments, the BCC treated according to the present invention is present on the trunk, extremities, hands or feet.

The size of the lesion may vary. In one embodiment, the BCC is less than about 2 cm. In another embodiment, the BCC is greater than about 2 cm, greater than about 3 cm, greater than about 4 cm, greater than about 5 cm or greater than about 6 cm. Lateral delimitation of the lesion may be aided by dermoscopy and deep demarcation can be estimated by biopsy and/or imaging techniques.

The BCC may be primary, incompletely excised or recurrent. In a particular embodiment, the BCC is not primary. The BCC may be nodular or infiltrating in exemplary embodiments.

The BCC may be, with respect to recurrence, a low-risk, moderate-risk or high-risk BCC.

In one embodiment, the BCC treated according to the present invention is a low-risk BCC in terms of recurrence, based on location or size or both. In a particular embodiment, the lesion is in a low-risk location and < 20 mm in size; in a moderate-risk location and < 10 mm in size; or in a high-risk location and < 6 mm in size. The lesion may also be considered low-risk in view of the borders, i.e., well-defined.

In another embodiment, the BCC treated according to the present invention is a high risk (or higher risk) BCC in terms of recurrence, based on location or size or both. In a particular embodiment, the lesion is in a low-risk location and ≥ 20 mm in size; in a moderate-risk location and ≥ 10 mm in size; or in a high-risk location and ≥ 6 mm in size. The lesion may also be considered high-risk in view of the borders, i.e., poorly-defined, or because it is recurrent.

About 20% of skin cancers develop from squamous cells- flat, scale-like cells that make up most of the epidermis. SCC is more likely to spread to other parts of the body than BCC, although far less than melanoma.

The most common risk factor, like BCC, is cumulative exposure to UV radiation. Other risk factors include light coloring (e.g., blue eyes, blonde hair), chemical carcinogenesis, chronic radiation dermatitis, HPV, xeroderma pigmentosa and oculocutaneous albinism.

SCC may arise de novo or be preceded by actinic keratosis (AK). There is a known conversion rate of about 0.0003 to about 0.05%. Histologically, AK is distinguished from SCC because the former involves only part of the epidermis. SCC *in situ* involves the full thickness of the epidermis and is well-defined and characterized by erythematous, scaly papules or plaques. Invasive SCC further involves penetration of the basement membrane of the epidermis and is characterized by indurated, scaling papules or plaques. Invasive SCC may be classified as well, moderately or poorly differentiated- where degree of differentiation is correlated with aggressiveness.

In one embodiment, the method of the present invention may be used to treat SCC. In a particular embodiment, the SCC is preceded by AK.

In another particular embodiment, the SCC is *de novo*, i.e., the patient has not been previously diagnosed with AK.

In one embodiment, the method of the present invention is used to treat SCC *in situ*.

In another embodiment, the method of the present invention is used to treat invasive SCC. In a particular embodiment, the method is used to treat invasive SCC selected from the group comprising well differentiated SCC, moderately differentiated SCC and poorly differentiated SCC.

The location of the lesion may vary. In exemplary embodiments, the SCC treated according to the present invention is present on the head, neck or face. In one embodiment, the SCC is present at a target site selected from the nose, cheek, periorbital area, auricular area, ear, temple, forehead or scalp.

The size of the lesion may vary. In one embodiment, the size of the SCC is less than about 2 cm. In another embodiment, the size of the SCC is greater than about 2 cm, greater than about 3 cm, greater than about 4 cm, greater than about 5 cm or greater than about 6 cm.

The thickness of the lesion may vary. In one embodiment, the thickness of SCC is less than about 2 mm. In another embodiment, the thickness of the SCC is greater than about 2 mm, greater than about 4 mm, greater than about 6 mm or greater than about 6 mm. In exemplary embodiments, the SCC is beyond subcutaneous fat or characterized by perineural invasion (PNI).

The SCC may be primary, incompletely excised or recurrent. In a particular embodiment, the SCC is not primary. In exemplary embodiments, the SCC is loco-regionally recurrent (LRR).

The SCC may be, with respect to recurrence, a low-risk, moderate-risk or high-risk SCC.

In one embodiment, the SCC treated according to the present invention is a low-risk SCC in terms of recurrence, based on location or size or both. In a particular embodiment, the lesion is in a low-risk location and < 20 mm in size; in a moderate-risk location and < 10 mm in size; or in a high-risk location and < 6 mm in size. The lesion may be also be considered low-risk in view of the borders, i.e., well-defined, or because it is well-differentiated or has a depth of < 2 mm.

In another embodiment, the SCC treated according to the present invention is a high risk

(or higher risk) SCC in terms of recurrence, based on location or size or both. In a particular embodiment, the lesion is in a low-risk location and ≥ 20 mm in size; in a moderate-risk location and ≥ 10 mm in size; or in a high-risk location and ≥ 6 mm in size. The lesion may also be considered high-risk in view of the borders, i.e., poorly-defined, or because it is recurrent. The lesion may also be considered high risk because it is poorly differentiated or has a depth of > 2 mm.

Other non-melanoma skin cancers that can be treated according to the methods of the present invention include including Merkel cell carcinoma, cutaneous (skin) lymphomas, Kaposi sarcoma, skin adnexal tumors, and sarcomas.

Acne. In a further embodiment, the skin disease or disorder is acne. Acne is a common skin condition which can occur anywhere on the body, but often on the face and back. It typically occurs during puberty, but can occur at any age. Without treatment, dark spots and scars can appear on the skin as acne clears.

Acne may be caused by one factor, or a combination of factors, which generally include genetic predisposition, Excessive production of sebum by the sebaceous glands, alterations of the keratinization process with abnormal desquamation of the sebaceous follicular epithelium, proliferation of *Propionibacterium* acnes and release of skin inflammatory mediators.

Acne can be classified as non-inflammatory or inflammatory. Non-inflammatory acne generally includes whiteheads (typically small and remaining under the skin) and blackheads (typically visible).

Inflammatory acne includes papules (small, usually pink bumps), pustules (red at their base and have pus at the top), nobules (large, solid, painful pimples that are embedded deep in the skin) and cysts (painful and filled with pus). Factors contributing to inflammation include bacterial infection (*Propionibacterium* acnes), free fatty acids and sebum, pro-inflammatory mediators (IL-1a, IL-b, TNF) and debris.

Representative, non-limiting types of acne that can be treated by the methods disclosed herein include acne vulgaris, acne comedo, papular acne, premenstrual acne, preadolescent acne, acne venenata, acne cosmetica, pomade acne, acne detergentica, acne excoriee, gram negative acne, pseudofolliculitis barbae, folliculitis, perioral dermatitis, hidradenitis suppurativa, cystic acne, acne atrophica, bromide acne, chlorine acne, acne conglobata, acne detergentica, epidemic

acne, acne estivalis, acne fulminans, halogen acne, acne indurata, iodide acne, acne keloid, acne mechanica, acne papulosa, pomade acne, premenstrual acne, acne pustulosa, acne scorbutica, acne scrofulosorum, acne urticata, acne varioliformis, acne venenata, propionic acne, acne excoriee, gram negative acne, steroid acne, nodulocystic acne and acne rosacea.

A grading system may also be used to categorize the various stages of the acne lesion. Grade one, the microcomedone, can appear as whiteheads or blackheads. Grade two is a papule, i.e., a small pink inflamed bump. Grade three is a pustule lesion with more visible inflammation than papule. Grade four is a nodule or large painful solid lesion that extends deep into the skin. Grade five is an inflamed lesion, very large and painful.

In one embodiment, the disease or disorder treated according to the method of the present invention is acne. In exemplary embodiment, the disease or disorder is inflammatory acne on the face, neck or portion thereof. The inflammatory acne may be mildly inflammatory, moderately inflammatory or severely inflammatory.

In one embodiment, the disease or disorder treated according to the method of the present invention is mild acne. Mild acne is generally categorized by the appearance of with blackheads and whiteheads, but can also include papules and pustules.

In another embodiment, the disease or disorder treated according to the method of the present invention is moderate acne. Moderate acne is generally characterized by appearance of more painful, deep-rooted, inflamed lesions, which can result in scarring.

In a further embodiment, the disease or disorder treated according to the present invention is severe acne. Severe acne is generally characterized by the appearance of deep-rooted inflammatory lesions, including cysts and nodules which can be painful and can produce scarring.

In one embodiment, the disease or disorder treated according to the present invention is not severe acne.

In one embodiment, the subject treated for acne according to the present invention is an adolescent. In another embodiment, the subject is an adult.

Porokeratosis. In one embodiment, the method of the present invention is used to treat prokeratosis. Porokeratosis is a clonal disorder of keratinization characterized by one or more atrophic patches surrounded by a clinically and histologically distinctive hyperkeratotic ridgelike

border called the cornoid lamella.

The method of the present invention may be used to treat any form of prokeratosis. Various forms are recognized including classic porokeratosis of Mibelli (PM); disseminated superficial porokeratosis (DSAP), disseminated superficial prokeratosis (DSP); linear porokeratosis, prokeratosis palmaris et plantaris disseminata (PPPD) and punctate porokeratosis, which might represent a variant of PPPD. Other less common forms are also recognized in the literature.

In exemplary embodiments, the method of the present invention is used to treat DSAP. In exemplary embodiments, the method of the present invention is used to treat PM.

In certain embodiments, the method of the present invention is used to treat multiple lesions simultaneously.

Heating

Heat by administered to the skin by any suitable thermal delivery device. The skin should be clean and dry. The device may be configured for direct application to the skin, or to provide heat indirectly. The energy source may be, for example, electrical, chemical, a laser, a microwave or radiofrequency. Representing, non-limiting thermal delivery devices include heating pads, heating masks, space heaters or infrared heaters.

In one embodiment, the affected area is the face and the thermal delivery device is a heat mask. In exemplary embodiments, the heat mask is a sodium acetate mask that heats upon crystallization. Crystallization is typically triggered by flexing a small flat disc of notched ferrous metal embedded in the super saturated sodium acetate liquid. In exemplary embodiments, the mask is covered with two layers of 2 play poly plastic paper.

In another embodiment, the affected area is the extremities and the thermal delivery device is a heating pad. The heating pad may be placed in any suitable manner.

In certain embodiments, a space heater is used to heat the facial skin, e.g., placing a space heater on a stand with wheels. The subject controls the skin heating at an ideal distance (adjusting for comfort) warming the skin. In this embodiment, the subject should wear protective eye wear (e.g., goggles).

In one embodiment, the skin is not heated by simply heating the room itself.

The temperature to which the thermal delivery device is heated may vary, depending on the disease or disorder being treated and the location. In one embodiment, the thermal delivery device is heated to a temperature of between about 20 to about 50°C, or more particularly, about 20 to about 30°C, about 30 to about 40°C, or about 40 to about 50°C.

In one embodiment, the disease or disorder is a pre-cancerous or cancerous lesion on the face and the thermal delivery device is heated to a temperature between about 38 and about 42°C, or more particularly, about 40°C.

In another embodiment, the disease or disorder is a pre-cancerous or cancerous lesion on the extremities and the thermal delivery device is heated to a temperature between about 38 and about 42°C, or more particularly, about 39°C.

In exemplary embodiments, the skin is heated to the temperature of the thermal delivery device. In exemplary embodiments, the temperature of the skin at the surface is less than the temperature to which the thermal delivery device is heated.

In one embodiment, the skin is heated to a surface temperature of between about 20 to about 50°C, or more particularly, about 20 to about 30°C, about 30 to about 40°C, or about 40 to about 50°C.

In another embodiment, the skin is heated to a surface temperature of greater than about 37°C. In a particular embodiment, the skin is heated to a surface temperature greater than about 38, greater than about 39, greater than about 40, greater than about 41 or greater than about 42°C.

In one embodiment, the skin is heated to a surface temperature between about 38 and about 42°C, or more particularly, about 40°C.

In another embodiment, skin is heated to a surface temperature between about 38 and about 42°C, or more particularly, about 39°C.

The duration of exposure to heat may vary. In one embodiment, the duration of exposure is between about 1 and about 90 minutes, or more particularly, between about 1 and about 10 minutes, about 10 and about 20 minutes, about 20 and about 30 minutes, about 30 and about 40 minutes, about 40 and about 50 minutes, about 60 and about 70 minutes, about 70 and about 80

minutes, or about 80 and about 90 minutes or more.

In another embodiment, the duration of exposure to heat is about 5 minutes, about 10 minutes, about 15 minutes, about 20 minutes, about 25 minutes, about 30 minutes, about 35 minutes, about 40 minutes, about 45 minutes, about 50 minutes, about 55 minutes, about 60 minutes, about 65 minutes, about 70 minutes, about 75 minutes, or about 80 minutes or greater.

In a particular embodiment, the skin disease or disorder is a pre-cancerous lesion and the duration of exposure to heat is about between about 20 and about 40 minutes, or more particularly, about 30 minutes.

In yet another embodiment, the skin disease or disorder is acne and the duration of exposure to heat is between about 20 and about 40 minutes, or more particularly, about 30 minutes.

Without being bound by any particular theory, it is believed that heating increases the one or more of: The rate of porphyrin production in the skin, the absorption of the photosensitive agent or the area of treatment surrounding the lesion so as to create a margin of treatment around the lesion.

In exemplary embodiments, the rate of porphyrin production in the skin is increased by about 10, about 20, about 30, about 40 or about 50% or more by heating as disclosed herein.

In exemplary embodiments, absorption is increased by about 10, about 20, about 30, about 40 or about 50% or more by heating as disclosed herein. The absorption may reflect an increased ratio of photosensitive agent absorption: lesion depth or and increased ratio of photosensitive agent absorption to lesion width. In a particular embodiment, the ratio is between about 0.5:1 to about 1:1, more particularly, about 0.5:1, about 0.6:1, about 0.7:1, about 0.8:1, about 0.9:1 or about 1:1 or greater.

In exemplary embodiments, the area of treatment is increased by about 10, about 20, about 30, about 40 or about 50% or more by heating as disclosed herein.

Optionally, the method may comprise one or more additional pre-treatment steps, i.e., before application of the photosensitive agents. In one embodiment, the pre-treatment may comprise curettage, dermoabrasion (e.g. with sandpaper) or micro-perforation of the skin.

Photosensitizing Agents/Composition

The present invention involves application of a photosensitizing agent(s) to skin, which accumulates in the affected area to a much higher degree than they accumulate in surrounding normal tissues. When photosensitizing agents are irradiated with an suitable dose of light, the activated agents pass on their energy to surrounding molecular oxygen to produce reactive oxygen species (ROS) in cells that have retained the agent. When an appropriate dose of light is utilized, the result is cell death.

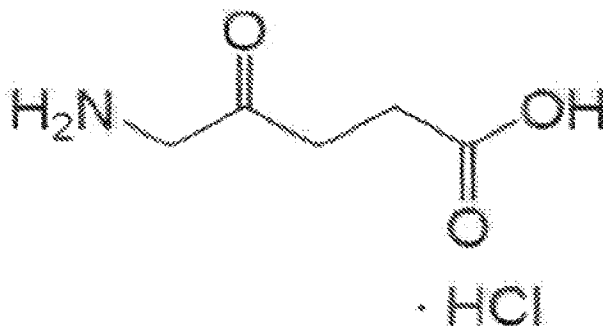
Photosensitizing agents can be administered orally or parenterally, neat or in combination with conventional pharmaceutical carriers.

Any suitable photosensitizing agent can be used in the method of the present invention. Numerous photosensitive agents are known in the art. In one embodiment, the photosensitizer is selected from the group consisting of porphyrins, chlorophylls, and dyes.

Non-limiting examples of photosensitive agents suitable for use in the present invention include phthalocyanines, porphyrins, porphyrin precursors, porphycenes, naphthalocyanines, phenoselenazinium, hypocrellins, perylenequinones, texaphyrins, benzoporphyrin derivatives, azaporphyrins, purpurins, Rose Bengal, xanthenes, porphycyanines, isomeric porphyrins, pentaphyrins, sapphyrins, chlorins, benzochlorins, hypericins, anthraquinones, rhodanols, barbituric acid derivatives, expanded porphyrins, dipyrromethenes, coumarins, azo dyes, acridines, rhodamine, azine derivatives, tetrazolium derivatives, safranines, indocyanines, indigo derivatives, indigo triazine derivatives, pyropheophorbides, pyrrole derived macrocyclic compounds, naturally occurring or synthetic porphyrins, naturally occurring or synthetic chlorins, naturally occurring or synthetic bacteriochlorins, naturally occurring or synthetic isobacteriochlorins, naphthalocyanines, phenoxazine derivatives, phenothiazine derivatives, chalcorganapyryllium derivatives, triarylmethane derivatives, rhodamine derivatives, fluorescein derivatives, verdin derivatives, toluidine blue derivatives, methylene blue derivatives, methylene violet derivatives, Nile blue derivatives, Nile red derivatives, phenazine derivatives, pinacyanol derivatives, plasmocorin derivatives and indigo derivatives, and combinations thereof.

In one embodiment, the photosensitizing agent is a porphyrin. In one embodiment, the porphyrin is selected from the group consisting of hematoporphyrins, metalloporphyrins, porphycenes, pheophorbides, purpurins, chlorins, protoporphyrins and phthalocyanines.

In a particular embodiment, the photosensitizing agent is 5-aminolevulinic acid (ALA) or a derivative or modification thereof. 5-aminolevulinic acid (also known as 5-aminolaevulinic



acid, delta- aminolevulinic acid, delta-aminolaevulinic acid, or 5-amino4-oxopentanoic acid) is an intermediate in the pathway to the production of the photosensitizer, protoporphyrin IX (PpIX).

5-aminolevulinic acid HCL

ALA can be used in the form of a salt, such as a HCL, or in a pharmaceutically equivalent form, such as an amide or ester. As used herein the term "ALA" refers to all of the above-referenced compounds.

In one embodiment, the photosensitizing agent is a non-porphyrin agent. In a particularly embodiment, the non-porphyrin agent is selected from the group consisting of anthraquinone, phenothiazine, psoraleans, anthracyclines, chalcogenopyrlium dyes, xanthene, cyanine, and curcuminoid sensitizers.

The photosensitizing agent can be administered in pure form, applied after being dissolved in a non-toxic solvent, or it can be administered in a topical formulation.

When formulated as a pharmaceutical composition, the composition contains a pharmaceutically acceptable carrier and optionally, one or more of the following agents: buffers, co-solvents, adsorbents, permeation enhancers, surfactants, stabilizers, emulsifiers, preservatives, chelating agents, thickening agents, smoothing agents, humectants or polymers.

The amount of the photosensitizing agent in the pharmaceutical composition (e.g., topical dosage form) may vary. In one embodiment, the photosensitizing agent is present in an amount from about 0.1 wt. % to about 75 wt. %, and more particularly, about 1.0 wt. % to about 40 wt. %, about 2.0 wt. % to about 30 wt. %, about 5.0 wt. % to about 25 wt. %, about 10 wt. % to about 20 wt. %, about 8 wt. %, about 10 wt. %, about 12 wt. %, about 14 wt. %, about 16 wt. %, about 18 wt. %, about 20 wt. % or about 22 wt. %.

In a particular embodiment, the amount of the amount of the photosensitizing agent in the pharmaceutical composition is greater than about 10 wt. %.

In a particular embodiment, the amount of the photosensitizing agent in the pharmaceutical composition is about 20 wt. %.

In another embodiment, the amount of the photosensitizing agent in the pharmaceutical composition is less than about 20 wt. %, and more particularly, less than about 15 wt. % or about 10 wt. % but in each case greater than zero.

In one embodiment, the photosensitizing agent is formulated for topical delivery. Topical dosing forms can include creams, gels, ointments, pastes, suspensions, lotions, foams, sprays, aerosols, and solutions.

The term "cream" refers to semi-solid emulsion systems which contain both an oil and water. Oil in water creams are water miscible and are well absorbed into the skin, Aqueous Cream BP. Water in oil (oily) creams are immiscible with water and, therefore, more difficult to remove from the skin. These creams are emollients, lubricate and moisturize, e.g., Oily Cream BP. Both systems require the addition of either a natural or a synthetic surfactant or emulsifier.

The term "ointment" refers to systems which have oil or grease as their continuous phase. Ointments are semi-solid anhydrous substances and are occlusive, emollient and protective. Ointments restrict transepidermal water loss and are therefore hydrating and moisturizing. Ointments can be divided into two main groups-fatty, e.g., White soft paraffin (petrolatum, Vaseline), and water soluble, e.g., Macrogol (polyethylene glycol) Ointment BP.

The term "lotion" refers to those solutions typically used in dermatological applications.

The term "gel" refers to semi-solid permutations gelled with high molecular weight polymers, e.g., carboxypolymethylene (Carbomer BP) or methylcellulose, and can be regarded

as semi-plastic aqueous lotions. They are typically non-greasy, water miscible, easy to apply and wash off, and are especially suitable for treating hairy parts of the body.

In one embodiment, the photosensitive agent is formulated as a gel. Pharmaceutically acceptable gelling agents suitable for use in the topical gel composition are those agents which provide viscosity to a formulation such that the formulation can be effectively applied to the affected area, including but not limited to hydroxypropylcellulose (e.g. Klucel H A), hydroxypropyl methylcellulose carrageenans, microcrystalline cellulose, carbomer, alginates, gellan gum, xanthan gum, veegum, hydroxyethylcellulose, guar gum and carbomers

The gel can further include local anesthetics and analgesics, such as camphor, menthol, lidocaine, dibucaine, and pramoxine; antifungals, such as ciclopirox, chloroxylonol, triacetin, sulconazole, nystatin, undecylenic acid, tolnaftate, miconazole, clotrimazole, oxiconazole, griseofulvin, econazole, ketoconazole, and amphotericin B.

The gel can also include one or more antiseptics, such as iodine, povidine-iodine, benzalkonium chloride, benzoic acid, nitrofurazone, benzoyl peroxide, hydrogen peroxide, hexachlorophene, phenol, resorcinol, and cetylpyridinium chloride.

The pH of the gel formulations of the photosensitizing agents are preferably within a physiologically acceptable pH range, e.g., within the range of about 4.5 to about 7.5, more preferably, of about 5.0 to about 6.5, such as a pH of about 5.1, 5.15, 5.2, 5.25, 5.3, 5.35, 5.4, 5.45, 5.5, 5.55, 5.6, 5.65, 5.7, 5.75, 5.8, 5.85, 5.9, 5.95, 6.1, 6.15, 6.2, 6.25, 6.3, 6.35, 6.4, 6.45, or 6.5. To stabilize the pH, preferably, an effective amount of a buffer is included. Acids or bases can be used to adjust the pH as needed.

The gel composition can be prepared by mixing the ingredients of the composition according to known methods in the art, for example methods provided by standard reference texts such as: Remington. The Science and Practice of Pharmacy, 1577-1591, 1672-1673, 866-885 (Alfonso R. Gennaro ed., 19th ed., 1995); Ghosh, T. K. et al., Transdermal And Topical Drug Delivery Systems (1997), both of which are hereby incorporated herein by reference.

In an exemplary embodiment, the photosensitizing agent is formulated as a gel comprising 20% aminolevulinic acid hydrochloride gel. In a particular embodiment, the pharmaceutical composition is LEVULAN® KERASTICK®, a topical formulation of 20% 5-aminolevulinic acid hydrochloride. In another particular embodiment, the pharmaceutical

composition is not LEVULAN® KERASTICK®.

In a further embodiment, the photosensitizing agent is formulated as a gel comprising 10% aminolevulinic acid hydrochloride. In a particular embodiment, the pharmaceutical composition is AMULEZ® (from Biofrontera), a non-sterile topical formulation of 10% 5-aminolevulinic acid hydrochloride (equaling 7.8% of free acid) in a gel-matrix with nanoemulsion.

In one embodiment, the the photosensitizing agent is in unit dosage form, such that the photosensitizing agent can be sub-divided in unit dose(s) containing appropriate quantities of the compound.

The quantity of photosensitizing agent to be administered depends on the choice of agent, the condition to be treated, the mode of administration, the individual subject, and the judgment of the practitioner. Depending on the specificity of the preparation, smaller or larger doses may be needed. In one embodiment, one gram (78mg) of 5-aminolevulinic acid hydrochloride gel (ALA) is administered.

The time between application of heat to the affected area and application of the photosensitizing agent may vary. This is known as the "heat-to-drug interval" and may be measured in seconds, minutes, hours or even days.

In one embodiment, the heat-to-drug interval is about 1 to about 60 seconds, or more particularly, about 1 to about 10 seconds, about 10 to about 20 seconds, about 20 to about 30 seconds, about 30 to about 40 seconds, about 40 to about 50 seconds, or about 50 to about 60 seconds.

In another embodiment, the heat-to-drug interval is about 1 to about 60 minutes, and more particularly, about 0.1 to about 1 minute, about 1 minute to about 5 minutes, about 5 minutes to about 10 minutes, about 10 minutes to about 20 minutes, about 20 minutes to about 30 minutes, about 30 minutes to about 40 minutes, about 40 minutes to about 50 minutes, or about 50 minutes to about 60 minutes.

In further embodiment, embodiment, the heat-to-drug interval is about 1 and about 24 hours, more particularly, about 1 to about 4 hours, about 4 to about 8 hours, about 8 to 12 hours, about 12 to about 16 hours, about 16 to about 20 hours, or about 20 to about 24 hours.

The composition can be administered in a suitable manner, preferably topical. A topical

composition may be administered in any suitable manner, e.g., rubbed on, poured on, applied with an applicator (e.g., a gauze pad, a swab, a bandage, etc.), or the like. In some cases, the composition can be a liquid, a gel, a cream, a lotion, an ointment, a solid "stick," or the like, that can be applied to the skin by hand, for example, by rubbing or spraying.

In exemplary embodiments, the affected area is the site of a precancerous or cancerous lesion, for example, on the face or neck. In some embodiments, the affected area is an area that covers the site of the precancerous or cancerous lesion and is, for example, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, or 50 cm in diameter. In some embodiments, the suitable location is an area where cancer prevention is desired. In other embodiments, the suitable location is a site where a pre-cancerous or cancerous lesion has previously been removed and the method is designed to prevent reoccurrence. In yet another embodiment, the suitable location is a site where a pre-cancerous or cancerous lesion has previously been incompletely removed.

In exemplary embodiments, the affected area is the site of an acne lesion, for example, on the face. In some embodiments, the affected area is an area that covers the site of the acne and is, for example, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, or 50 cm in diameter. In some embodiments, the suitable location is an area where acne prevention is desired.

The duration of exposure to the photosensitive agent may vary. In one embodiment, the duration of exposure is between about 1 and about 30 minutes, or more particularly, about 1, about 5, about 10, about 15, about 20, about 25 or about 30 minutes.

In exemplary embodiments, the duration of exposure to the photosensitive agent may be less while achieving the same effect due to pre-heating of the skin. In one embodiment, the duration of exposure is about 10, about 30, about 30, about 40, about 50 or about 60%, about 70%, about 80%, or about 90% while achieving the same effect.

In a particular embodiment, the duration of exposure to the photosensitive agent is about 1 hour, about 45 minutes, about 30 minutes or less than about 30 minutes.

Incubation Time

One advantageous feature of the present invention is the reduction it permits in incubation time for the photosensitive agent. The FDA approval for PDT for AK requires a 14 hour incubation with ALA before exposure to the blue light. Yet, for many clinicians, that creates a burden including extended duration of treatment.

In one embodiment, the incubation time is reduced by greater than about 10%, greater than about 15%, greater than about 20%, greater than about 25%, greater than 30%, greater than about 35%, greater than 40%, greater than about 45%, greater than about 50%, greater than about 54%, greater than 60%, greater than about 65%, greater than 70%, greater than about 75% or greater than 80%.

In another embodiment, the incubation time is reduced by between about 10% and about 70%, about 20% and about 60%, about 30% and about 50%.

In a particular embodiment, the incubation time is reduced by greater than 30% while achieving equivalent results to a photoactive agent incubated for about 14 hours.

In another particular embodiment, the incubation time is reduced by greater than 20% while achieving equivalent results to a photoactive agent incubated for about 5 hours.

In another particular embodiment, the incubation time is reduced by greater than 10% while achieving equivalent results to a photoactive agent incubated for between about 1 and about 3 hours, or more particular, about 3 hours, about 2 hours or about 1 hour.

In another embodiment, the incubation time is less than 14 hours, less than 13 hours, less than 12 hours, less than 11 hours, less than 10 hours, less than 8 hours, less than 7 hours, less than 6 hours, less than 5 hours, less than 4 hours, less than 3 hours, less than 2 hours or less than 1 hour.

In a further embodiment, the incubation time is about 1 hour, about 2 hours, about 3 hours, about 4 hours, about 5 hours, about 6 hours, about 7 hours or about 8 hours or more.

In exemplary embodiments, the incubation time is less than about 1 minute, less than about 45 seconds, less than about 30 seconds, less than about 25 seconds, less than about 20 seconds, less than about 15 seconds or less than about 10 seconds.

In exemplary embodiments, the incubation time is about 30 seconds, about 25 seconds, about 20 seconds, about 18 seconds, about 16 seconds, about 14 seconds, about 12 seconds or about 10 seconds or less.

In exemplary embodiments, the photosensitizing agent is incubated simultaneously with application of heat to the skin or within a few seconds or minutes prior to heating of the skin or after heating of the skin has begun.

Light

After the skin has been heated and the photosensitizer applied, the area to be treated is then irradiated with light of a proper wavelength and sufficient power in the presence of oxygen to activate the photosensitive agent, resulting in reactive oxygen species. These reactive oxygen species react with biomolecules, fatally damaging some of the cells in the treatment area.

The step of irradiating generally comprises the step of providing a light source that is activated to produce the light. The light source may be an artificial or natural light source (e.g., sunlight).

The light can be provided by a laser, light emitting diode (LED), or other light source known to those skilled in the art (e.g., chemiluminescent light source). The light can be provided by a single source, or a plurality of light sources can be used.

In an exemplary embodiment, the light source is an LED lamp.

The amount and wavelength of radiation applied is dependent on the nature of the photosensitizing agent used. Preferably, the wavelength is selected to correspond with or at least overlap the excitation wavelength(s) of the photosensitizing agent. Even more preferably, the wavelength matches the excitation wavelength of the photosensitizing agent and has low absorption by the non-target cells or tissues.

The wavelength is typically within the wavelengths of visible and near infra-red light, which includes wavelengths from about 320 nm to about 780 nm. However, specific photosensitizers typically respond to light having a particular wavelength.

In one embodiment, the light administered to the affected area is blue light. Blue light has a wavelength between about 380 nm and 500 nm, with visible blue light having a wavelength of about 475 nm. The dominant wavelength of the blue light used in the method of the present invention may vary. In one embodiment, it is between about 450 and about 475 nm. In a particular embodiment, it is about 450 nm, about 455 nm, about 460 nm, about 465 nm, about 470 nm or about 475 nm. The source of the blue light may vary. In one embodiment it is Blu-U® from DUSA Pharmaceuticals.

In one embodiment, the light is not blue light. In a particular embodiment, the light is not Blu-U®.

In another embodiment, the light is not blue light and the photosensitive agent is not LEVULON® KERASTICK®.

In another embodiment, the light is red light. Red light has a wavelength from about 620 to about 750 nm. The dominant wavelength of the red light used in the method of the present invention is between about 630 nm and about 640 nm, or more particularly about 635 nm. The source of the red light may vary. In one embodiment, it is BF-RhodoLED[®] (from BioFrontera).

In certain embodiments, the administration of light is continuous.

In exemplary embodiments, the light source is disposed external to an intact skin layer of the subject.

In other embodiment, more than one administration of light can be used within a single treatment, e.g., two, three, four or more discrete administrations. The amount of light applied in the two more administrations may be the same or different. Once the first application of light has been applied to the effective area, a sufficient interval of time should be allowed to pass for an effective amount of the photosensitizing agent to further penetrate the tissue. The particular layer of skin targeted can vary depending on the disease being treated.

The duration of exposure to light may vary depending on the power of the radiation source. In one embodiment, the duration of exposure is between about 1 to about 30 minutes, or more particularly about 1 to about 5 minutes, about 5 to about 10 minutes, about 10 to about 15 minutes, about 15 to about 20 minutes, about 20 to about 25 minutes or about 25 to about 30 minutes or longer.

In another embodiment, the duration of exposure is about 1 minute, about 3 minutes, about 5 minutes, about 8 minutes, 10 minutes, about 12 minutes, about 15 minutes, about 18 minutes, or about 21 minutes, about 25 minutes, about 28 minutes, or about 31 minutes or more.

The light should be administered for a period of time and intensity sufficient to activate the photosensitizing agent. The amount of light energy necessary to obtain effective results can be pre-determined by evaluating the effective amounts for particular subjects, types of subjects, photosensitizers, and/or formulations. The amount of light energy can also be regulated in response to feedback during treatment. For example, the amount of light being delivered can be regulated based on concurrent analysis of photosensitizing agent penetration, heat level in the

tissue (e.g., skin), or the level of discomfort being experienced by the subject.

In one embodiment, the amount or "dose" ranges from about 5 to about 200 J/cm² or in particular, about 5 to about 10 J/cm², about 10 to about 20 J/cm², about 20 to about 30 J/cm², about 30 to about 40 J/cm² or about 40 to about 50.

In one embodiment, In one embodiment, the present invention provides a method of heat-enabled, low-dose PDT. By "low-dose PDT", it is meant a total photodynamic therapy experience at substantially lower levels of intensity of the radiation employed and the time of exposure to light (i.e., low-dose light). In one embodiment, the intensity of radiation employed is about 10, about 20, about 30, about 40, about 50, about 60 or about 70% less than prior art methods. In another embodiment, the amount of radiation is less than about 100 J/cm², less than about 80 J/cm², less than about 70 J/cm², or more particularly, less than about 65 J/cm², less than about 60 J/cm², less than about 55 J/cm², less than about 50 J/cm², less than about 45 J/cm², less than about 40 J/cm².

In another embodiment, the amount of radiation is less than about less than about 40 J/cm², or more particularly, the dose ranges from about 35 to about 40 J/cm², or more particularly, about 37 J/cm².

The fluence rate of the light may vary. In one embodiment, the light source has a fluence rate of between about 1 to about 100 mW/cm².

In the case of skin tissue, a sufficient interval of time is preferably provided to allow the photosensitizer to reach the lower levels of skin such as the basal epidermis and/or the papillary dermis, which is the upper layer of the dermis immediately beneath the epidermis. The particular layer of skin targeted can vary depending on the disease being treated. For example, the time interval can be 1 hour, 30 minutes, 10 minutes, 5 minutes, or any other interval within this range. In addition to providing sufficient time for the photosensitizer to penetrate the skin to the desired level, care should also be taken to avoid providing too much time, which can result in passage of significant amounts of the photosensitizing agent beyond the intended site.

Typically, the administration of photodynamic therapy comprises administering one or more sessions of therapy (e.g., one, two, three, four, or more sessions of therapy) to the subject. According to embodiments, a session includes both the administration of a photoreactive compound to a treatment area and the irradiation of the treatment area, which can occur over the

course of several hours or one or more days or weeks. According to other embodiments, a session comprises just irradiation of the treatment area alone. In some embodiments, the photodynamic therapy is administered in two sessions. In some embodiments, the photodynamic therapy is administered in only one session.

In exemplary embodiments, the method further comprises monitoring the disease or disorder of the skin following administration of photodynamic therapy according to the present invention wherein a lack of clinical response to the method is indicative that the method should be repeated and/or that the amount of the photosensitive agent and/or the dose of light should be increased. Monitoring may comprise visual inspection, palpation, imaging, assaying the presence, level, or activity of one or more biomarkers associated with the disease or disorder and/or clinical response in a sample obtained from the subject, or a combination of two or more of the foregoing. The monitoring is preferably done regularly, which for the purposes of this disclosure is at least several times a week and preferably about daily.

Where the disease or disorder is a non-melanoma skin cancer, monitoring may be directed to one or more of the following: tumor size, rate of change in tumor size, appearance of a new tumor (i.e., recurrence), rate of appearance of new tumors (i.e., rate of recurrence), change in a symptom of NMSC, appearance of a new symptom associated with the NMSC, quality of life or a combination of two or more of the foregoing.

In one embodiment, the method of the present invention reduces the recurrence of NMSC relative to the same method in the absence of a pre-heating step. In a particular embodiment, recurrence is reduced by about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45 or about 50% or more. In another particular embodiment, recurrence is less than about 10%, less than about 8%, less than about 6%, less than about 4% or less than about 2%. In another particular embodiment, recurrence is about 10, about 9.5, about 9, about 8.5, about 8, about 7.5, about 7, about 6.5, about 6, about 5.5, about 5, about 4.5, about 4, about 3.5, about 3, about 2.5, about 2, about 1.5, about 1.0, or about 0.5 or less. Recurrence may be measured at any suitable time point, such as, for example, about six months, about one year, about two years, about three years, about four years or about 5 years.

Without being bound by any particular theory, the method of the present invention is believed to permit improvement in determining the margin of the tumor. In one embodiment, the ability to determine a tumor margin is about 5, about 10, about 15, about 20, about 25, about 30,

about 35, about 40, about 45 or above 50% or more improved using the present method.

In another embodiment, the method of the present invention reduces the time to recurrence of NMSC relative to the same method in the absence of a pre-heating step. In a particular embodiment, time to recurrence is reduced by about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45 or about 50% or more. In another particular embodiment, the mean time to recurrence was reduced by about 1 to about 36 months, or more particularly, about 1, about 3, about 6, about 9, about 12, about 15, about 18, about 21, about 24, about 27, about 30, about 33 or about 36 months or more.

Advantageously, the method of the present invention permits improvement in the determinations of tumor margin relative to the same method in the absence of step (i). In exemplary embodiments, the ability to determine the tumor margin is improved about 5, about 10, about 15, about 20, about 25, about 30, about 40, about 45 or about 50% or more.

In exemplary embodiments, the method of the present invention permits treatment with accuracy as to margins consistent with conventional surgical treatment.

Where the disease or disorder is acne, monitoring may be directed to one or more of the following: acne lesion counts, acne lesion severity.

In one embodiment, the method of the present invention produces a decrease in mean acne lesion counts in a subject. In a particular embodiment, the percentage reduction is about 10 or more, about 20 or more, about 30 or more, about 40 or more, about 50 or more, about 60 or more, about 70 or more, about 80 or more, or about 90% or more.

In a particular embodiment, the method of the present invention produces a decrease in mean acne lesion counts in a subject of between about 40% and about 90%, more particularly, about 45% and about 85%, and even more particularly about 47% and about 80%.

The percentage reduction may increase as the method is carried out multiple times. For example, the decrease in mean acne lesions may be about 30% or more after a first treatment, about 40% or more after a second treatment and/or about 50% or more after a third treatment.

The result achieved by the method of the present invention may persist. For example, the decrease in mean acne lesion count may persist for about one, about two, about three, about four, about five, about six, about seven, about eight or about nine months or more. Persistence for

about twelve months or more may be considered clinical remission.

In one embodiment, a population of patients treated according to the method of the present invention has a decrease in acne lesion count relative to patients treated according to the same method in the absence of step (i). In a particular embodiment, the acne lesion count in the population treated according to the method of the present invention is decreased by about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50%, about 60%, about 70%, about 80% or about 90% or more relative to patients treated according to the same method in the absence of step (i).

In certain embodiments, the methods reduce acne lesion count in a period of time in the range of one to about twelve weeks. In some embodiments, the methods result in very few instances (e.g. <1%) of redness, dryness, and peeling of treated skin.

In another embodiment, a population of patients treated according to the method of the present invention has a decrease in acne lesion severity relative to patients treated according to the same method in the absence of step (i). In a particular embodiment, the acne lesion severity in the population treated according to the method of the present invention is decreased by about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50%, about 60%, about 70%, about 80%, about 90% or more relative to patients treated according to the same method in the absence of step (i).

The method of the present invention may result in diminished side effects relative to the same method in the absence of a pre-heating step prior to administration of the photosensitive agent. These side effects include, for example, discomfort, scaling, and sterile postulation.

In one embodiment, discomfort is reduced by about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80 or about 90% or more.

In another embodiment, scaling is reduced by about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80 or about 90% or more.

In yet another embodiment, sterile postulation is reduced by about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80 or about 90% or more.

In a particular embodiment, the method of the present invention provides a statistically significant two-point reduction in an Investigator's Global Assessment (IGA) of acne severity compared to vehicle control at six, nine or twelve weeks.

In another particular embodiment, the method of the present invention provides an absolute reduction in the number of acne lesions (non-inflammatory, inflammatory or both) of about 2, about 4, about 6, about 10, about 12, about 14, about 16, about 18, about 20, about 22 or about 24 or more.

In one embodiment, the method of the present invention decreases the risk of atrophic (depressed) acne scars. In a particular embodiment, the risk is reduced by about 10, about 20, about 30, about 40, about 50, about 60, about 70, about 80 or about 90% or more.

III. Combination Therapy

The present invention includes methods of treatment involving co-administration of one or more therapies in addition to the PDT with prior-heat treatment described above. As used herein, the terms "in combination" or "co-administration" can be used interchangeably to refer to the use of more than one therapy (e.g., one or more prophylactic and/or therapeutic agents). The use of the terms does not restrict the order in which therapies (e.g., prophylactic and/or therapeutic agents) are administered to a subject.

In exemplary embodiments, the method of the present invention may be used in combination with one or more agents used to treat actinic keratoses. Non-limiting examples of such agents include 5-fluorouracil (5-FU) and imiquimod (Aldara, Zyclara).

In exemplary embodiments, the method of the present invention may be used in combination with administration of one or more anti-cancer agents, such as cytotoxic agents, chemotherapeutic agents, anti-signaling agents, and anti-angiogenic agents.

In one embodiment, the method of the present invention may be used in combination with administration of one or more agents used to treat BCC. Non-limiting examples of such agents include imiquimod (Aldara, Zyclara), fluorouracil- topical (Efudex, Carac, Fluoroplex), vismodegib and sonidegib.

In one embodiment, the method of the present invention may be used in combination with administration of one or more agents used to treat SCC. Non-limiting examples of such agents include imiquimod (Aldara, Zyclara), fluorouracil- topical (Efudex, Carac, Fluoroplex), and cetuximab (Erbix).

In exemplary embodiments, the methods of the present invention may be used in combination with administration of one or more anti-acne agents. Non-limiting examples of

useful anti-acne actives include the keratolytics such as salicylic acid (o-hydroxybenzoic acid), derivatives of salicylic acid such as 5-octanoyl salicylic acid and 4-methoxysalicylic acid; retinoids such as retinoic acid and its derivatives (e.g., cis and trans); sulfur-containing D and L amino acids and their derivatives and salts, particularly their N-acetyl derivatives, a preferred example of which is N-acetyl-L-cysteine; lipoic acid; seboestats such as flavonoids and bioflavonoids; bile salts such as scymnol sulfate and its derivatives, deoxycholate, and cholate; abietic acid; adapalene; allantoin; aloe extracts; arbutic acid and its salts; aryl-2,4-dioxo oxazolidine derivatives; ASEBIOL® (available from Laboratories Serobiologiques, located in Somerville, N.J.); azaleic acid; barberry extracts; bearberry extracts; belamcanda chinensis; benzoquinolinones; benzoyl peroxide; berberine; BIODERMINE® (available from Sederma, located in Brooklyn, N.Y.); bioflavonoids; bisabolol; S-carboxymethyl cysteine; carrot extracts; cassia oil; clove extracts; citral; citronellal; climazole; CREMOGEN® M82 (available from Dragoco, located in Totowa, N.J.); cucumber extracts; dehydroacetic acid and its salts; dehydroepiandrosterone salicylate; dichlorophenyl imidazolidioxolan which is commercially available as COMPLETECH MBAC-OS® (from Lipo, located in Paterson, N.J.); DL valine and its esters; DMDM hydantoin; Epicutin TT (available from CLR); erythromycin; escinol; ethyl hexyl monoglyceryl ether; ethyl 2-hydroxy undecanoate; farnesol; farnesol acetate; geraniol; glabridin; gluconic acid; gluconolactone; glyceryl monocaprates; glycolic acid; grapefruit seed extract; guggulipid; Hederagenin (available from Maruzen); hesperitin; hinokitol; hops extract; hydrogenated rosin; 10-hydroxy decanoic acid; ichthyol; interleukin 1 alpha antagonists; iodo-2-propynyl butyl carbamate; Kapilarine (available from Greentech); ketoconazole; lactic acid; lemon grass oil; Lichochalcone LR15 (available from Maruzen); linoleic acid; LIPACIDE® C8CO (available from Seppic, located in Paris, France); lovastatin; 4-methoxysalicylic acid; metronidazole; minocycline; mukurossi; neem seed oil; vitamin B.sub.3 compounds (such as niacinamide and nicotinic acid); nisin; 5-octanoyl salicylic acid; octopirox; panthenol; 1-pentadecanol; peonia extract; peppermint extract; phelladendron extract; 2-phenyl-benzothiophene derivatives; phloretin; PHLOROGINE® (available from Secma); phosphatidyl choline; proteolytic enzymes; quercetin; red sandalwood extract; resorcinol; rosemary extract; rutin; sage extract; salicin; salicylic acid; skull cap extract; siber hegger extract; siberian saxifrage extract; silicol; sodium lauryl sulfate; sodium sulfoacetamide; Sophora Extract (available from Maruzen); sorbic acid; sulfur; sundar vati extract; tea tree oil; tetracycline; tetrahydroabietic acid; thyme extract; tiocolone; tocopherol; trehalose 6-

undecylenoate; 3 tridecene- 2-ol; triclosan; tropolone; UNITRIENOL® T27 (available from Unichem, located in Gouda, Netherlands); vitamin D.sub.3 and its analogs; white thyme oil; willow bark extract; wogonin; Ylang Ylang; zinc glycerolate; zinc linoleate; zinc oxide; zinc pyrithione; zinc sulfate and mixtures thereof.

In one embodiment, the methods of the present invention may be used in combination with administration of one or more "anti-inflammatory" compounds. Representative, non-limiting examples of anti-inflammatory compounds include azelaic acid, clindamycin, niacinamide, and tretinoin.

EXAMPLES

EXAMPLE 1: Treatment of Inflammatory and Cystic Acne

A total of six (6) patients were treated. The affected area was treated for about one (1) hour with a warming mask at 40°C, followed by application of 10% ALA gel and 37J/cm² of red light at 630 nm.

The results included a mild, sun-burn like reaction, followed by pustular eruption at day 3 and 95% clear at one (1) month. The result was sustained for at least six (6) months. See Figure 1, which shows baseline (Figure 1A) and results (clear) at three (3) months (Figure 1B). See also Figure 2, which shows results at baseline (Figure 2A), 1 hour (using poryphorin camera)(Figure 2B), three (3) days (Figure 3B) and six (6) weeks.

EXAMPLE 2: Treatment of Basal Cell Carcinoma on Extremities

Patients with nodular basal cell carcinoma were treated. The affected area was treated with a heating pad at 39°C. Each was also treated with 20% ALA gel without curettage. Blue light at 37J/cm² was applied at 410 nm.

A wide margin of poryphorins was detected. See Figure 3, including Figure 3B which shows a wide margin of pophyrins in the heated area.

EXAMPLE 3: Treatment of Basal Cell Carcinoma on Extremities

Patients with recurrent nodular and infiltrative basal cell carcinoma were treated. The affected area was treated with a heating pad at 40°C. Each was also treated for one (1) hour with 10% ALA gel following curettage. Red light at 630 nm of 37J/cm² was applied.

Results indicate that patients were clear for at least six (6) months with a single treatment. See

Figure 4, which shows baseline (Figure 4A), one (1) year following post curettage alone (Figure 4C) and six (6) months following treatment with PDT (Figure 4D).

EXAMPLE 4: Treatment of BCC on Scalp

Patients with infiltrative basal cell carcinoma of the scalp were treated. The affected area was heat treating using a 40°C heating pad. A 20 % ALA solution was applied for one hour, followed by 10 J/cm² of blue light at 417 nm.

Biopsy showed that lesions were clear one month following treatment (Figure 6B). Additional evidence shows lesions were clear up at one month (Figure 5), which persisted for sixteen (16) months following treatment.

EXAMPLE 5: Treatment of SCC-IS

Patients with SCC-IS were treated. The affected area was heat treated with a sodium acetate warming pad to 40°C. A 20% ALA solution was applied to each for 20 minutes. Blue light was applied at 417 nm for 10J/cm².

The results indicate that each was clear one (1) year following a single treatment. See Figure 7.

EXAMPLE 6: Treatment of Refractory Disseminated Porokeratosis with Related SCC

Patients with refractory disseminated porokeratosis with related SCC. The affected area was heat treated with a 40° C heating pad. 10% ALA gel was applied for one (1) hour. Red light was applied with an energy of 37J/cm² and a wavelength of 630 nm.

Results are shown in Figure 9, including baseline (Figure 9A), one (1) week (Figure 9B) and one (1) month (Figure 9C).

EXAMPLE 7: Treatment of Actinic Keratosis

Patients with actinic keratosis were treated. Heat was applied to the affected area using a 40° C warming mask. A 20% ALA solution was applied, following 20 minute incubation. Light was then applied.

Results are shown in Figure 10, including baseline (Figure 10A), twenty (20) minutes (Figure 10B), one (1) day (Figure 10C), one (1) week (Figure 10D) and two (2) months (Figure 10E). Significant porphyrins are shown.

EXAMPLE 8: Treatment of Actinic Keratosis

Heat was applied to the affected area using a 40° C warming mask. A 20% ALA solution was applied, following 30 minute incubation. Light was then applied.

Results are shown in Figure 11, including baseline (Figure 11A), thirty (30) minutes (Figure 11B), one (1) day (Figure 11C) and one (1) week (Figure 11D). Even greater porphyrins are shown.

EXAMPLE 9: Treatment of Actinic Keratosis

A 20% ALA solution was applied for one hour (room temperature 70F), following a 60 minute incubation. Light was then applied.

Results are shown in Figure 12, including baseline (Figure 12A) and one (1) hour. Minimal porphyrins are shown with no heat.

EXAMPLE 10: Treatment of Moderate Inflammatory and Pustular Acne

A one hour incubation with 10% aminolevulinic acid (ALA) with a sodium acetate warming mask (skin temperature 40C) followed by 37J/cm² 635nm red light was used to treat an index patient with moderate inflammatory and pustular acne on the face. The reduction in lesion counts was persistent 9 months after a single thermal PDT, as shown in Figure 17 and Table II.

Table I: Inflammatory and Non-Inflammatory Lesion Counts and Clearance Rates
Determined by a Blinded Investigator:

Visit	Inflammatory	Non-Inflammatory	Total Lesions	Percent Clearance
baseline	31	22	53	
1 month	14	7	21	60
3 months	10	13	23	57
9 months	6	4	10	81

EXAMPLE 11: Treatment of Moderate Inflammatory and Pustular Acne

A patient with moderate inflammatory and pustular acne on the face using a one hour incubation with 10% aminolevulinic acid with a sodium acetate warming mask (skin

temperature 40°C) followed by 37J/cm² 635nm red light. . Remodeling of acne scars is shown 9 months after single thermal PDT, as shown in Figure 18 and Table II.

TABLE II

Visit	Inflammatory Lesions with Potential to Scar	Scars Present
baseline	94	-
9 months	8	1

EXAMPLE 12: Treatment of Actinic Keratoses

Facial skin with actinic keratoses was treated with a 30 minute incubation with 20% ALA at 40C using a sodium acetate warming mask compared to a one hour incubation at room temperature (room temperature 70°F, skin temperature 30°C). Increased porphyrin was observed, as shown in Figure 23. Porphyrin images were captured using the VISIA-CR® 4.1 camera system and analyzed using the Image-Pro® Plus 7.0 (IPP®, Media Cybernetics Inc.) imaging analysis software. The intensity of PpIX fluorescence signals measured within the masked area was quantified on a scale of 0 to 255.

Table III:

	1 Hour Incubation 30C	30 Minutes 40C		
Mean Porphyrin Intensity	71.5402	131.2849		

CLAIMS

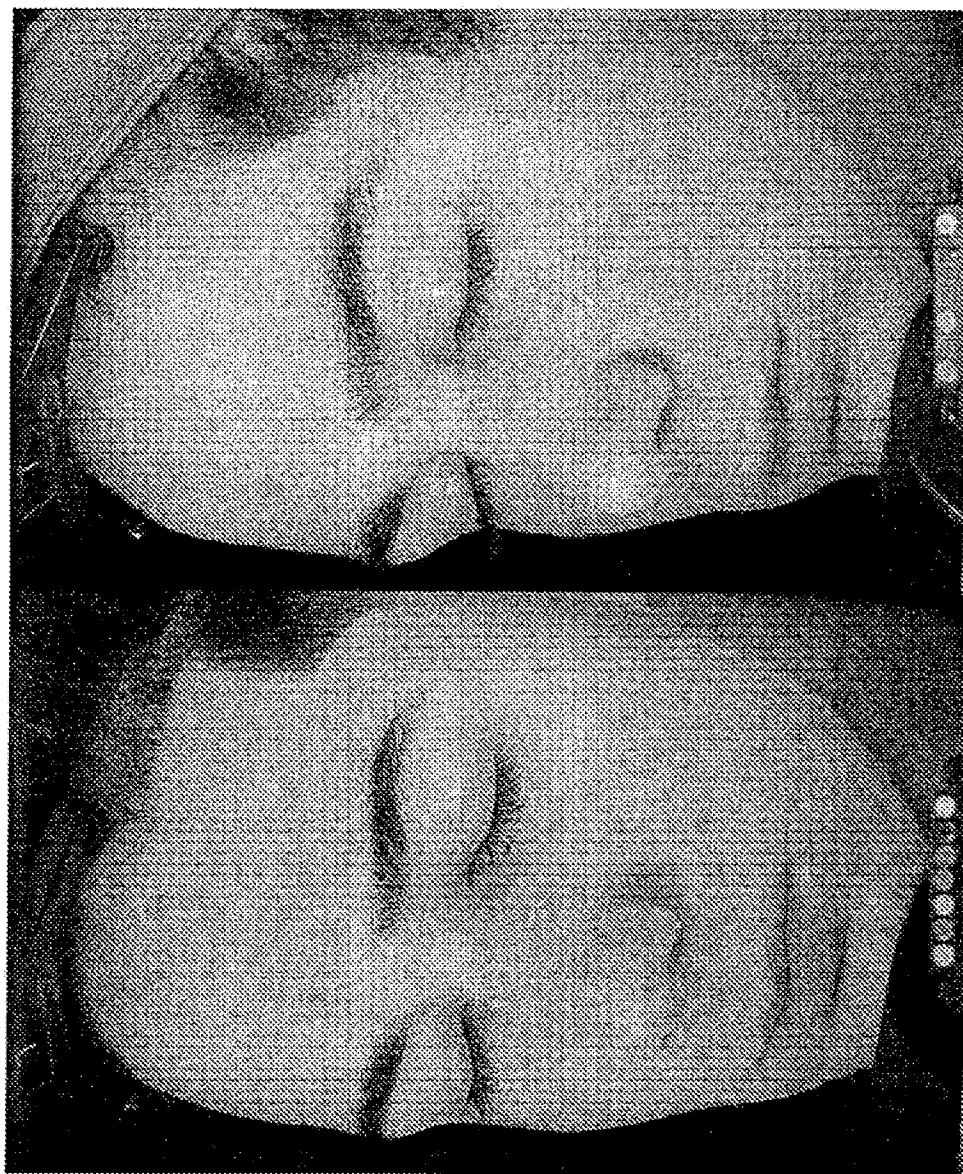
What is claimed is:

1. A method of treating facial acne in a subject in need thereof, comprising (i) administering heat to an affected area of the subject's skin using a thermal delivery device to achieve a temperature of between about 38 and about 42°C for a suitable time; (ii) incubating a pharmaceutical composition comprising at least one photosensitizing agent for an incubation period of less than about 14 hours to provide an incubated pharmaceutical composition; (iii) administering a therapeutically effective dose of the incubated pharmaceutical composition to the affected area for a suitable time period; (iii) administering a suitable dose of red light to the affected area, thereby treating the facial acne.
2. The method of claim 1, wherein the incubation time is less than about 10 hours.
3. The method of claim 1, wherein the incubation time is less than about 5 hours.
4. The method of claim 1, wherein the incubation time is less than about 3 hours.
5. The method of claim 1, wherein heat is applied using a sodium acetate mask.
6. The method of claim 1, wherein the wherein the heat is administered in (i) for about 60 minutes.
7. The method of claim 1, wherein the at least one photosensitizing agent is 5-ALA.
8. The method of claim 21, wherein the pharmaceutical composition is a gel.
9. The method of claim 1, wherein the pharmaceutical composition is a nano-emulsion.
10. The method of claim 7, wherein the 5-ALA is present at about 20 wt. % of the pharmaceutical composition.
11. The method of claim 27, wherein the 5-ALA is present at about 10 wt. % of the pharmaceutical composition.
12. The method of claim 1, wherein the wavelength of the red light is between about 625 and about 645 nm.
13. The method of claim 1, wherein the wavelength of the red light is about 630 nm.

14. The method of claim 1, wherein the dose of the red light is about 37 J/cm²
15. The method of claim 1, wherein the wavelength is about 630 nm at a distance of 6 cm from the subject's skin.
16. The method of claim 1, wherein the acne lesion count is reduced by greater than about 30% as a result of treatment.
17. The method of claim 1, wherein the acne lesion count is reduced by greater than about 50% as a result of treatment.
18. The method of claim 1, wherein the acne lesion count is reduced by greater than about 75% as a result of treatment.
19. The method of claims 16-18, wherein the reduction persists for at least about three months.
20. The method of claims 16-18, wherein the reduction persists for at least about six months.
21. The method of claim 1, wherein treatment produces less discomfort than the same method not employing step (i).
22. The method of claim 1, wherein treatment produces less scaling than the same method not employing step (i).
23. The method of claim 1, wherein treatment produces less sterile pustulation than the same method not employing step (i).
24. The method of claim 1, wherein the acne is mild acne.
25. The method of claim 1, wherein the acne is moderate acne.
26. The method of claim 1, wherein the acne is severe acne.
27. The method of claim 1, wherein the acne is inflammatory acne.

Fig 1

Inflammatory and cystic Acne:
1 hour 10% ALA gel 40C 37J/cm² 630nm red light



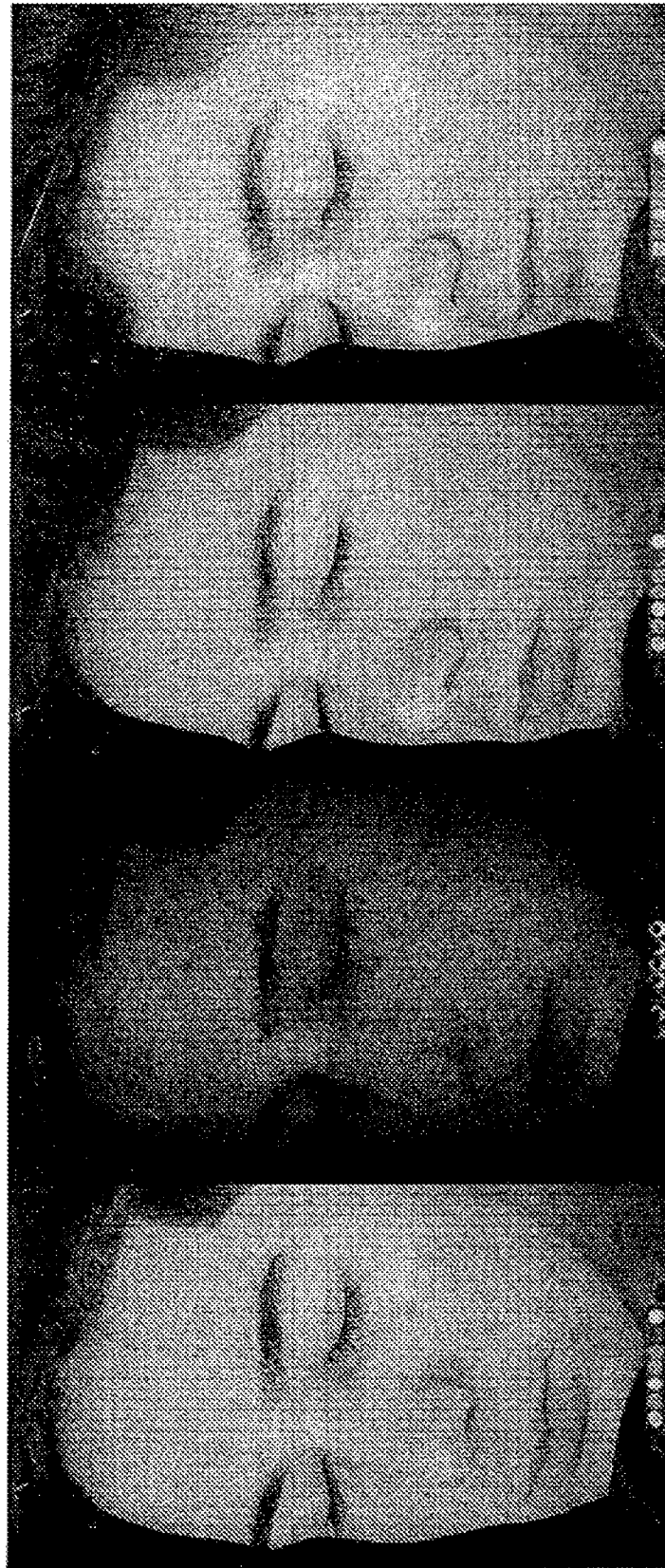
clear 3
months after
single
treatment

(still clear
6 months)

baseline (A) 3 months (B)

Fig. 2

Inflammatory and cystic Acne:
1 hour 10% ALA gel 40C 37J/cm² 630nm red light



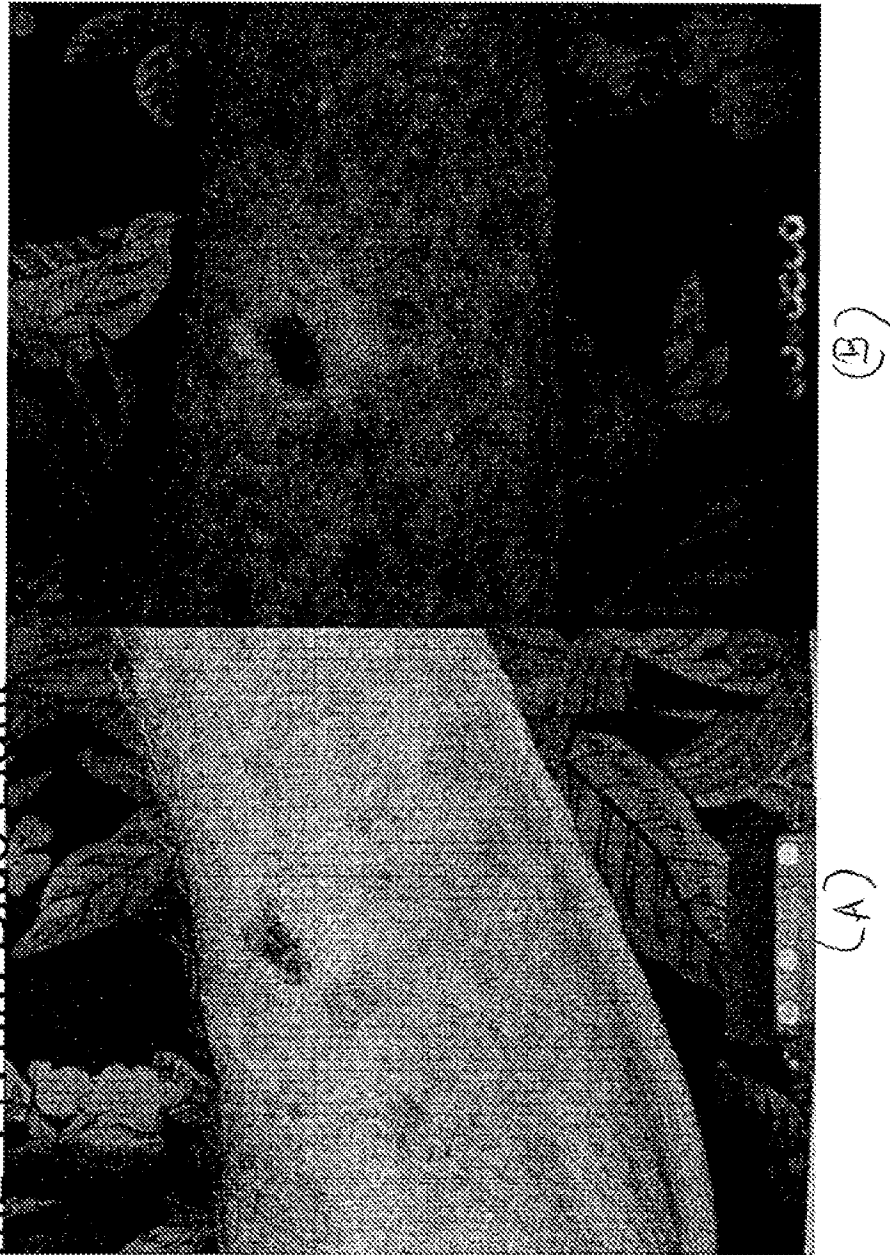
baseline
(A)

1 hour 40C
(B)

3 days
(C)

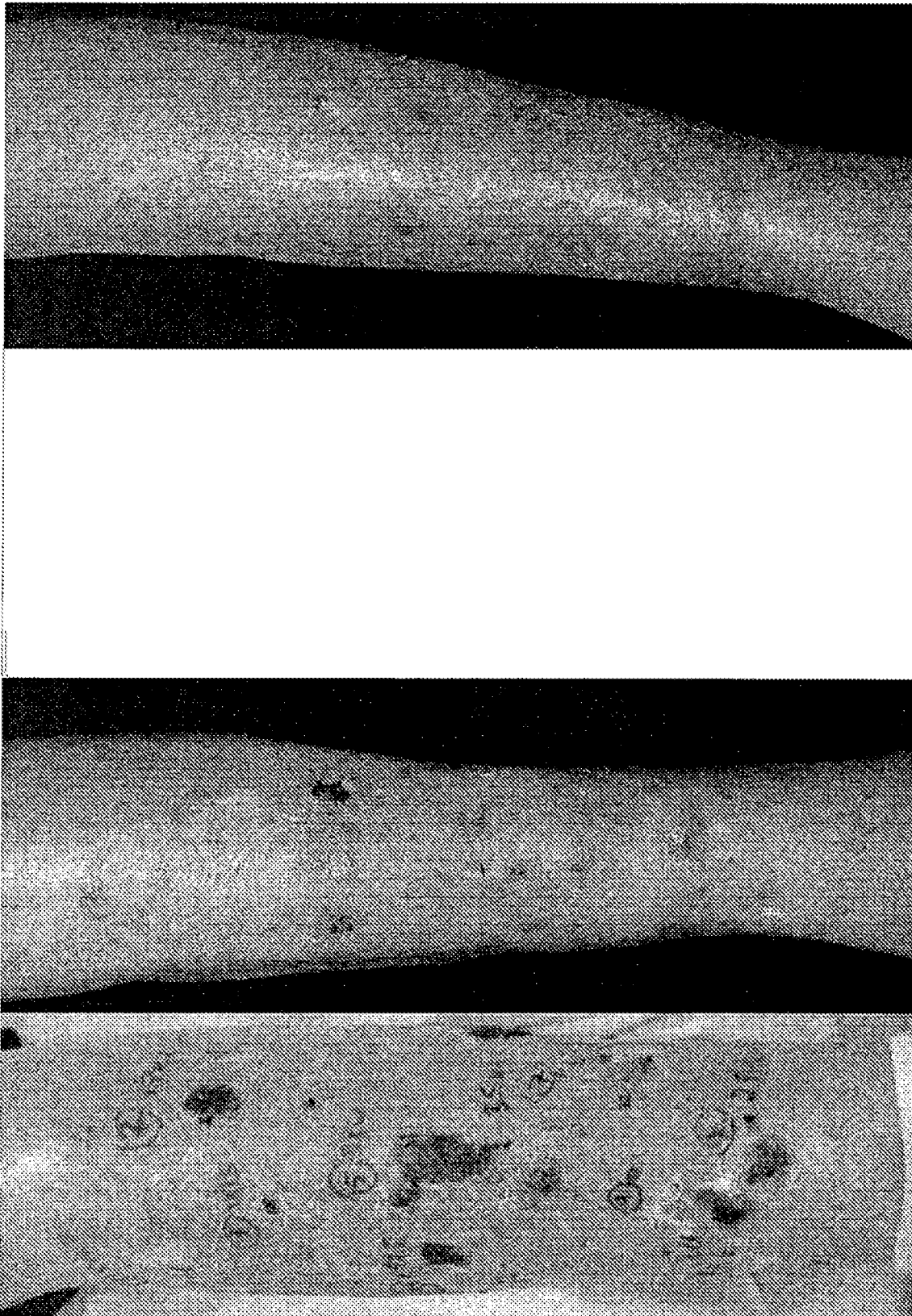
6 weeks
(D)

Fig. 3
Nodular BCC
1 hour 20% ALA solution (no curettage) 39C heating pad
set at medium
10J/cm² 417nm Blue Light



wide margin of porphyrins in heated area

Fig. 4



baseline
BCCs (A)

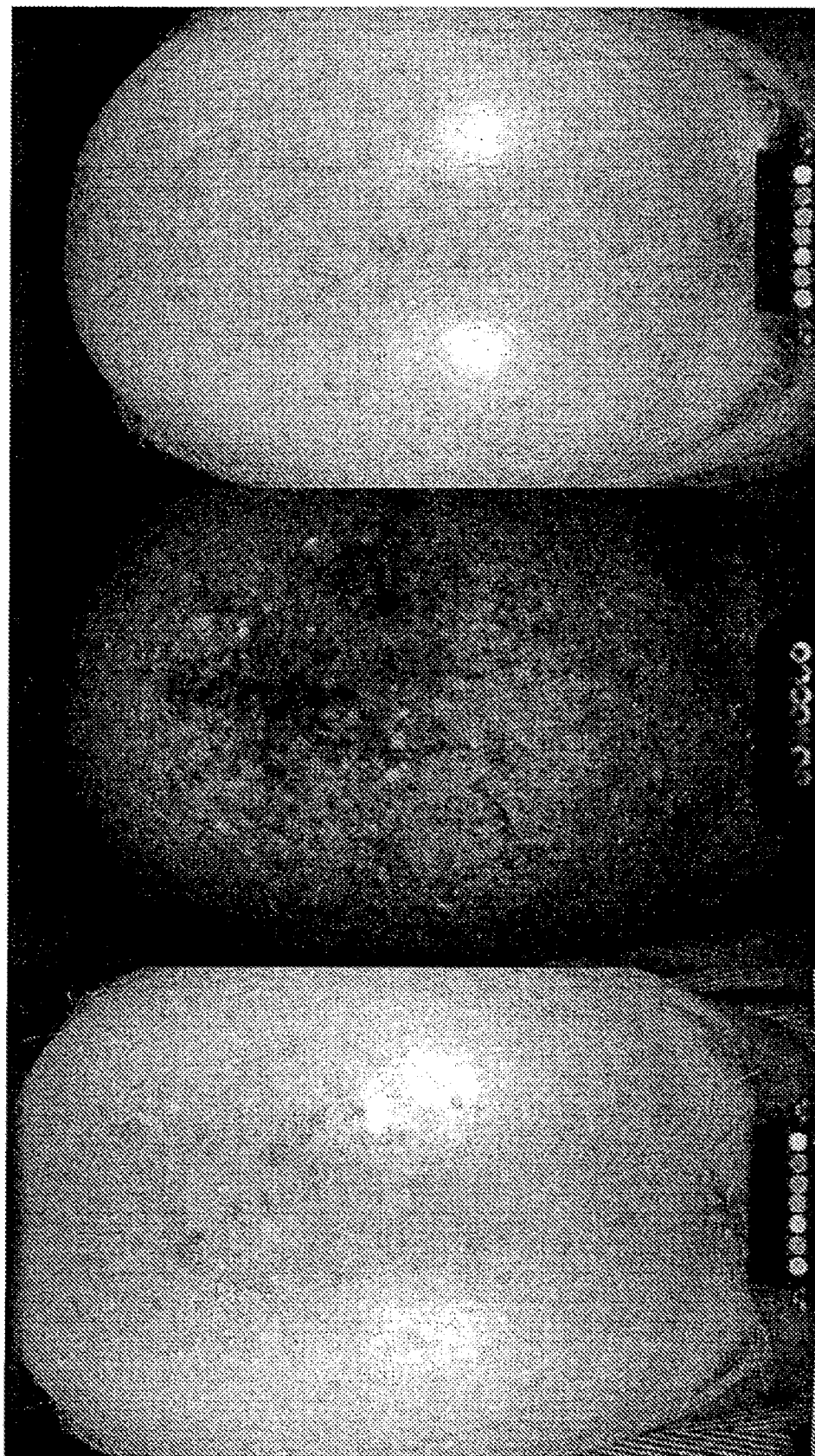
1 year post
curettage alone (B)

immediately
post PDT (C)

6 months
post PDT (D)

Fig. 5

BCC: 1 hour 20% ALA Solution 40C heating pad 10J/cm² 417nm blue light



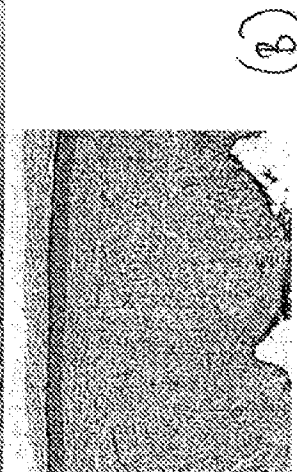
baseline

post 1 hour ALA 40C

1 mos

remains clear 16 months post treatment

Fig. 6
BCC: 1 hour 20% ALA Solution 40C heating pad 10J/cm² 417nm blue light



(A)

(B)

No residual BCC
1 month

Infiltrative BCC

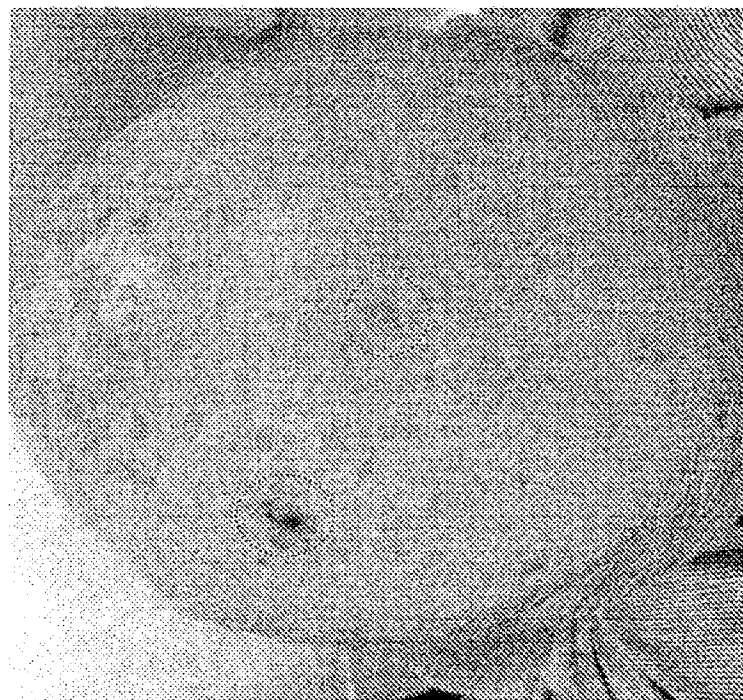
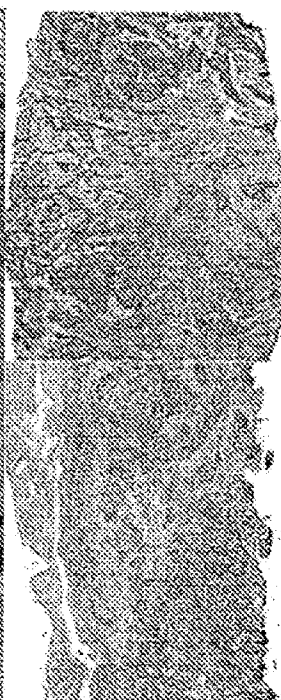
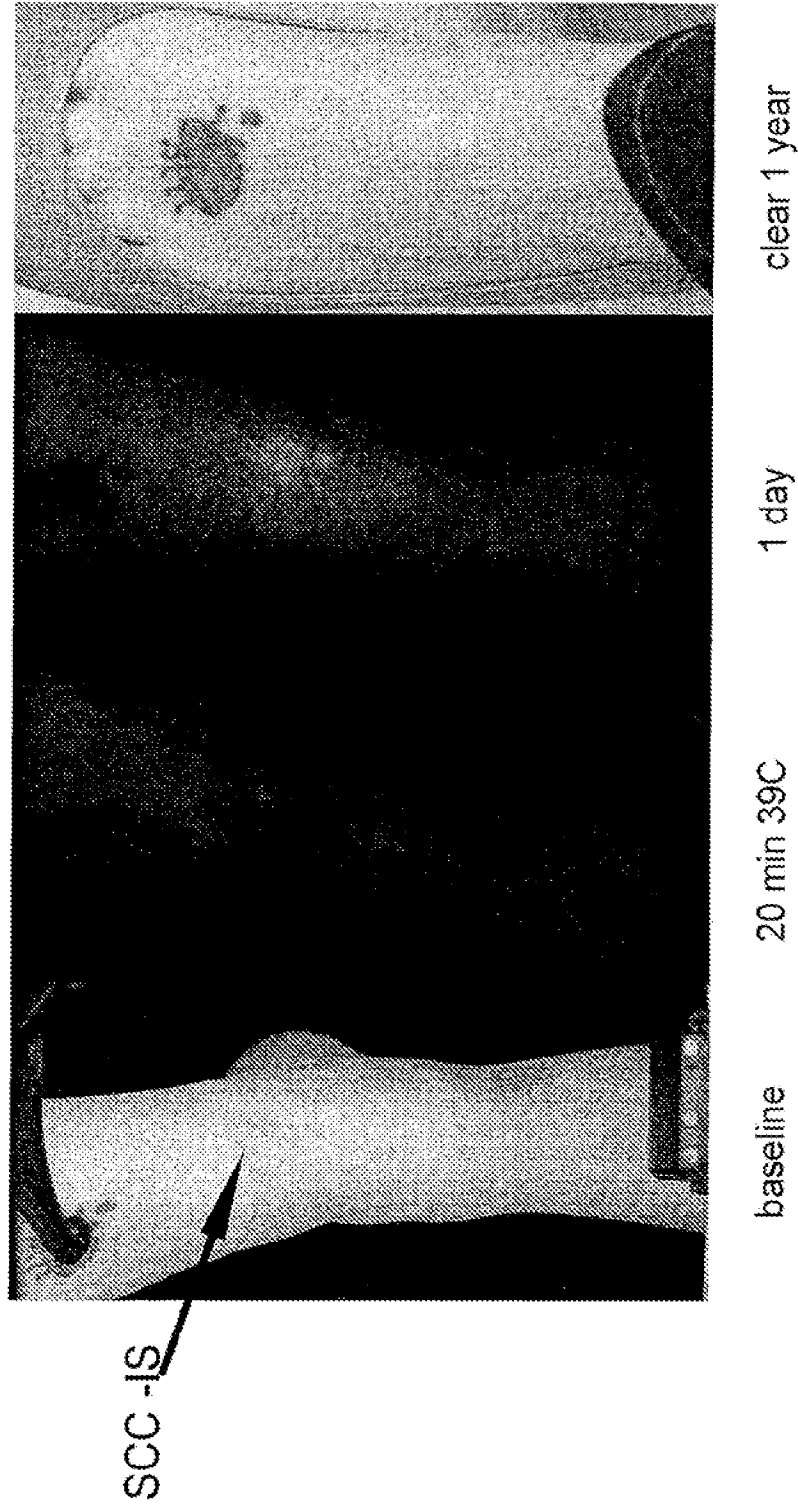


Fig. 7

20 min sodium acetate warming pad
ALA 20% Soln 10J/cm² 417 nm Blue Light PDT for SCC-IS



Heat creates margin of porphyrins around lesion by increasing area of absorption and increasing production of porphyrins in that area.

Fig. 8 multi focal BCC



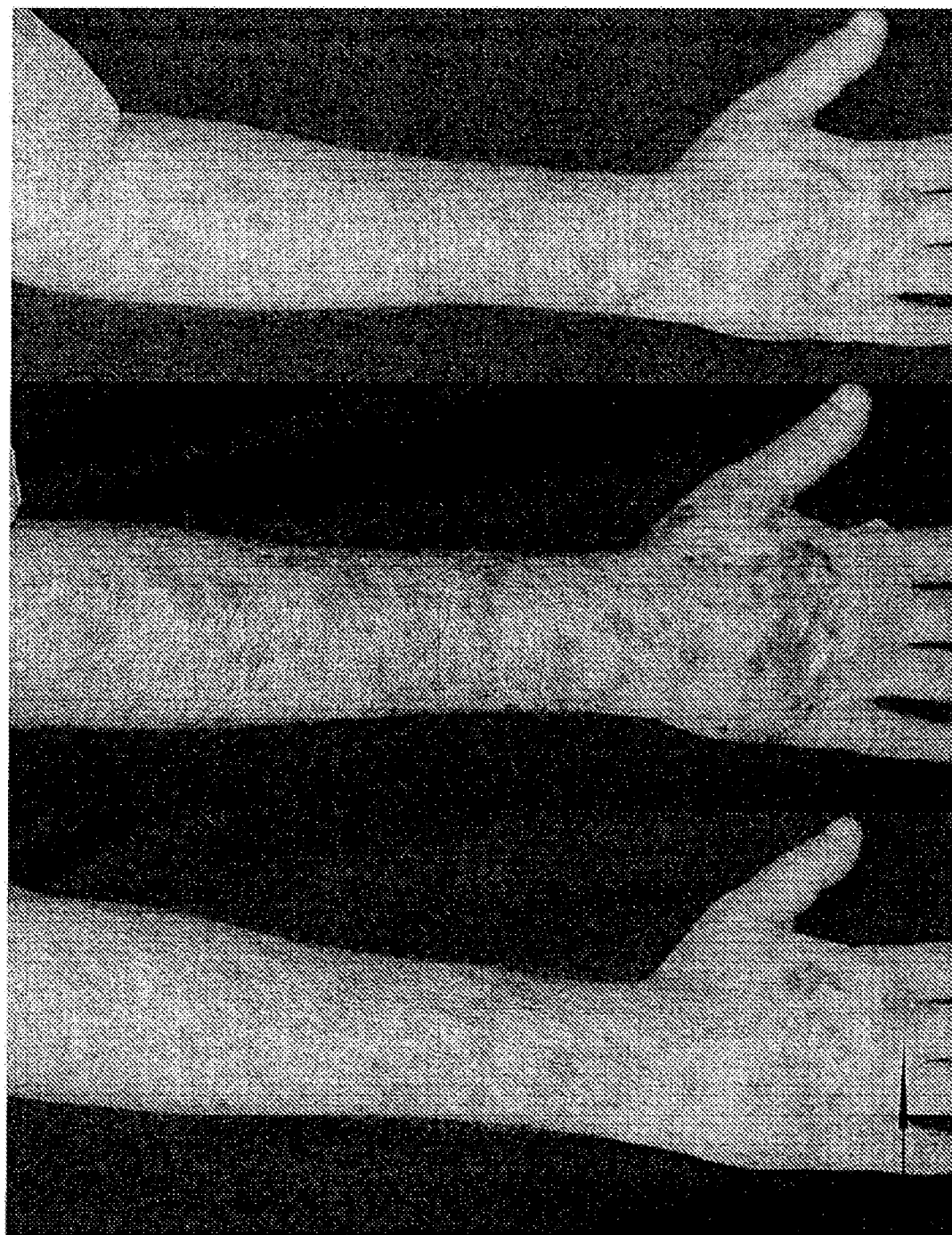
baseline

post 30 min 10% ALA gel 41C

wide margin porphyrins following 30 min 41C

Fig. 9

Refractory Disseminated Porokeratosis with Related SCC
1 hour 10% ALA gel 40C heating pad 37J/cm² 630nm Red Light



1 month

1 week

baseline

SCC post
Mohs and
FTSG

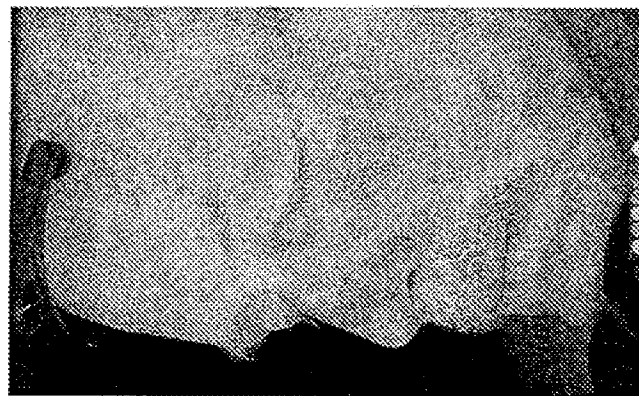
Fig. 10

20 min incubation ALA 20% soln 40C warming mask



baseline

(A)



20 min 40C

(B)

1 day

(C)

1 week

(D)

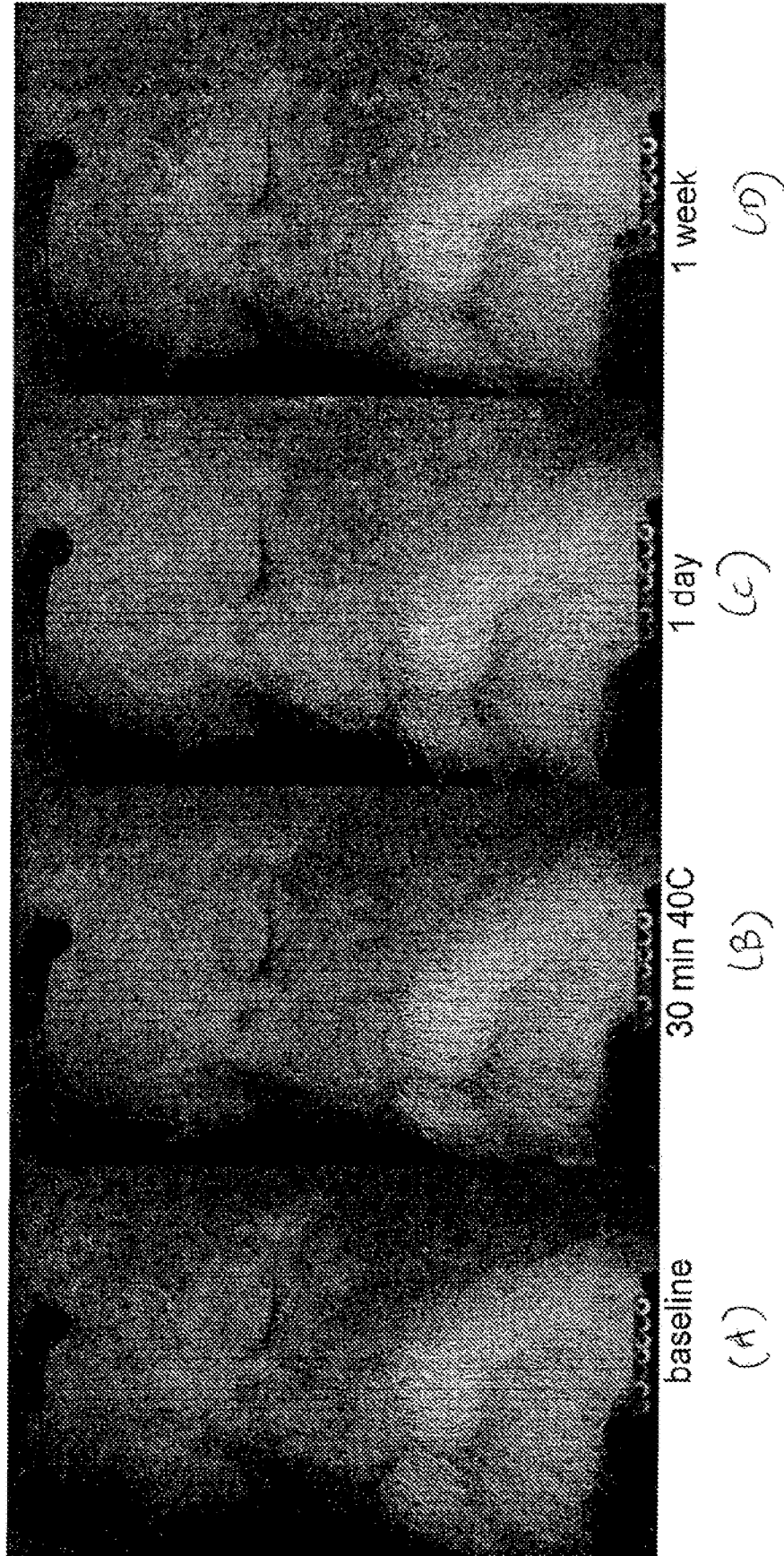
2 months

(E)

significant porphyrins with 20 min at 40C

Fig. 11

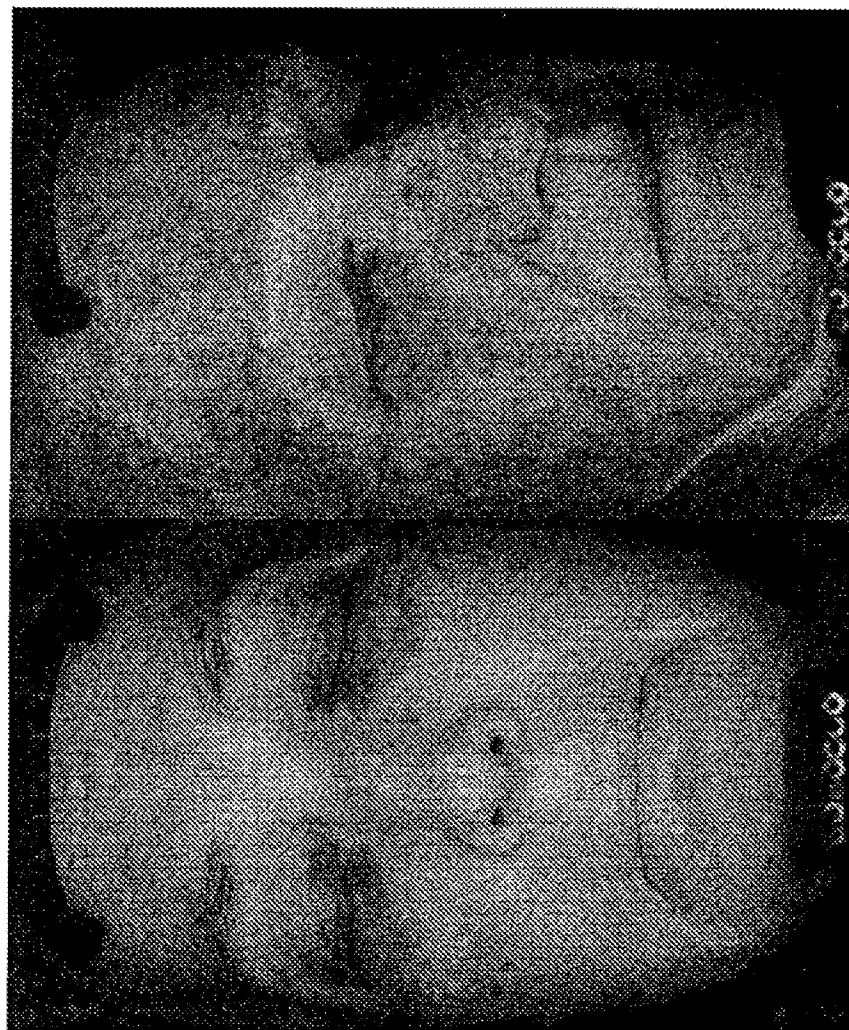
30 min incubation ALA 20% soln 40C warming mask



even greater porphyrins at 30 min at 40C

Fig. 12

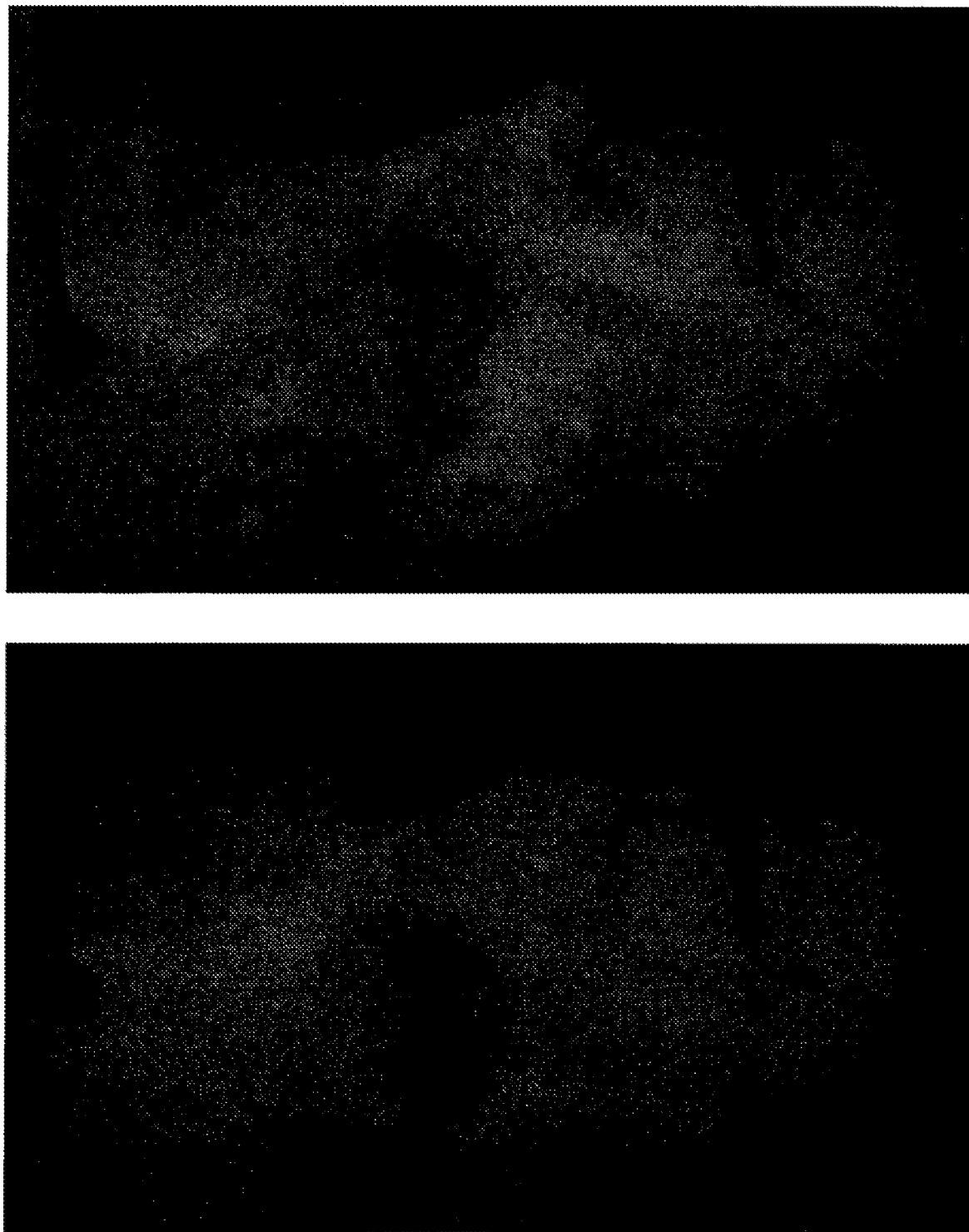
60 min incubation ALA 20% soln no heat



typical
porphyrins
1 hour ALA
(room 70F)

minimal porphyrins at one hour with no heat

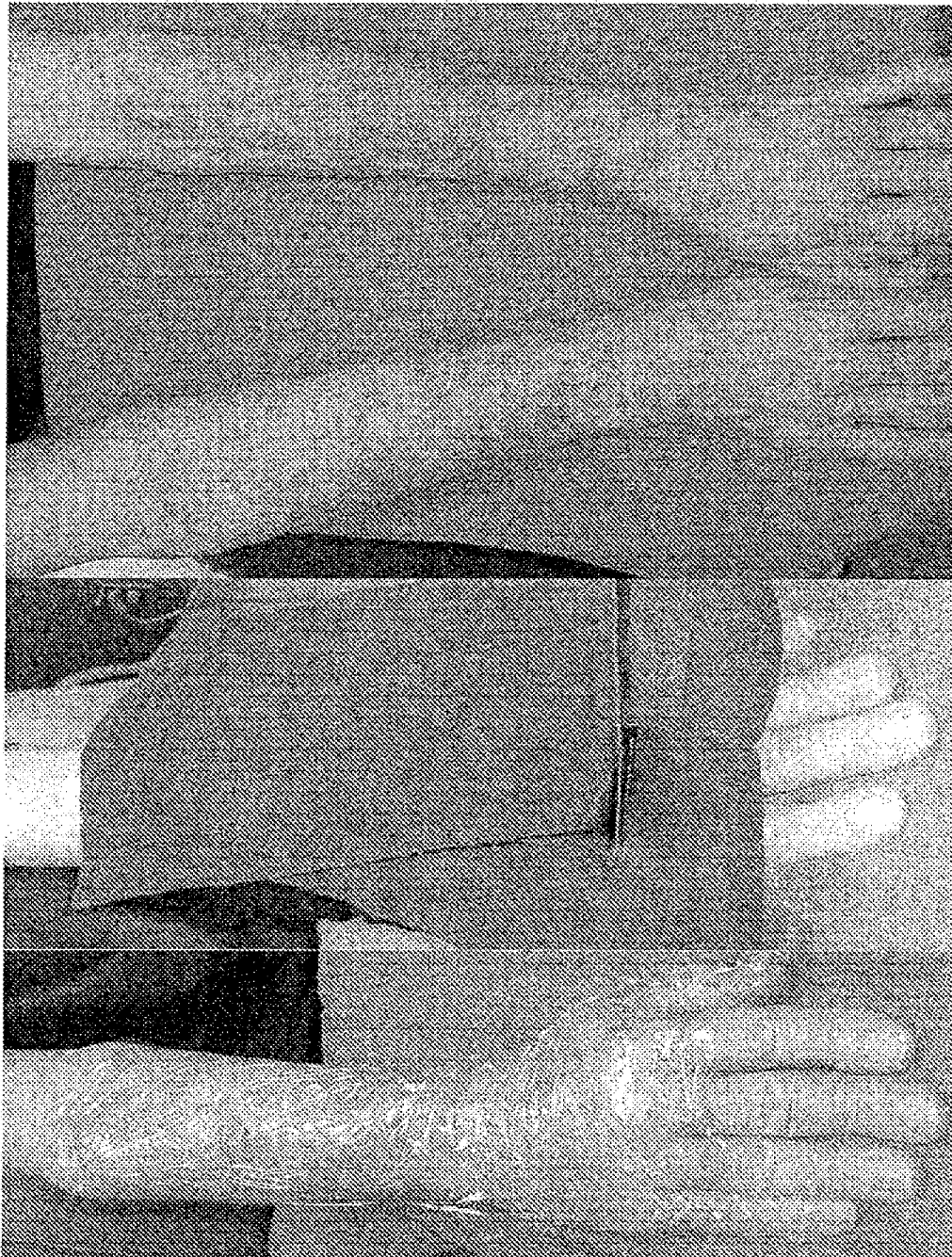
Fig. 13 Porphyrin Images During Simultaneous Incubation ALA 20% Solution



minimal porphyrins 1 hour

porphyrins 20 min 40C

Fig. 14



one hour
20% ALA soln
no heat

one hour
20% ALA sold
39C warm sand

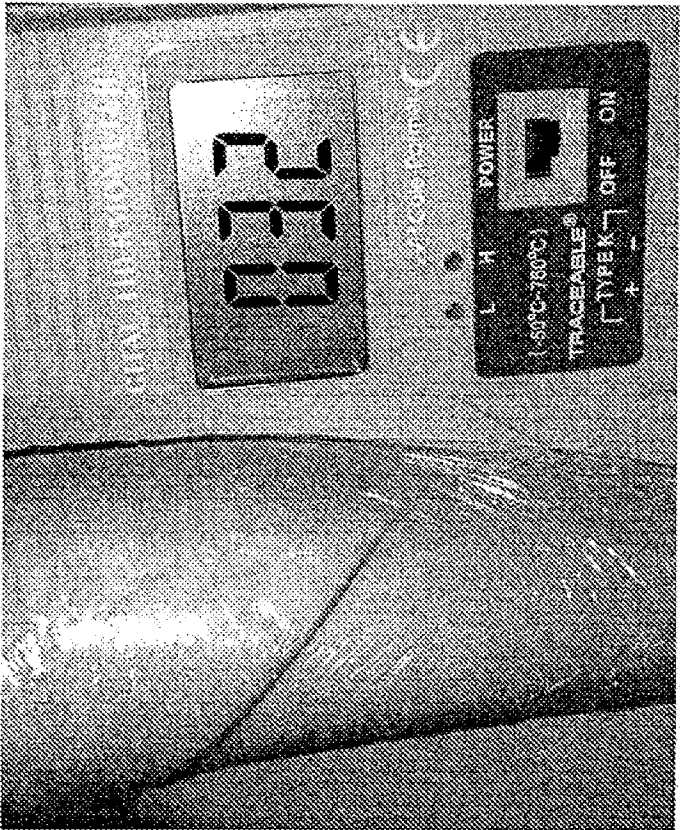
immediately post PDT
heated side shows
increased PDT reaction

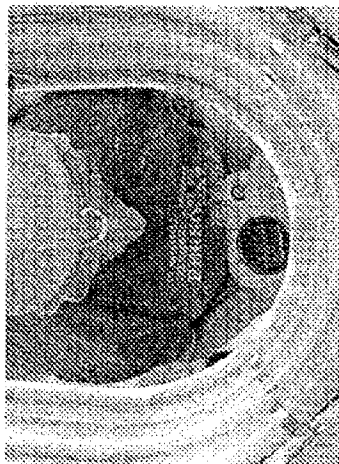
Fig. 15

Heating Pad

ambient T 20C 65%

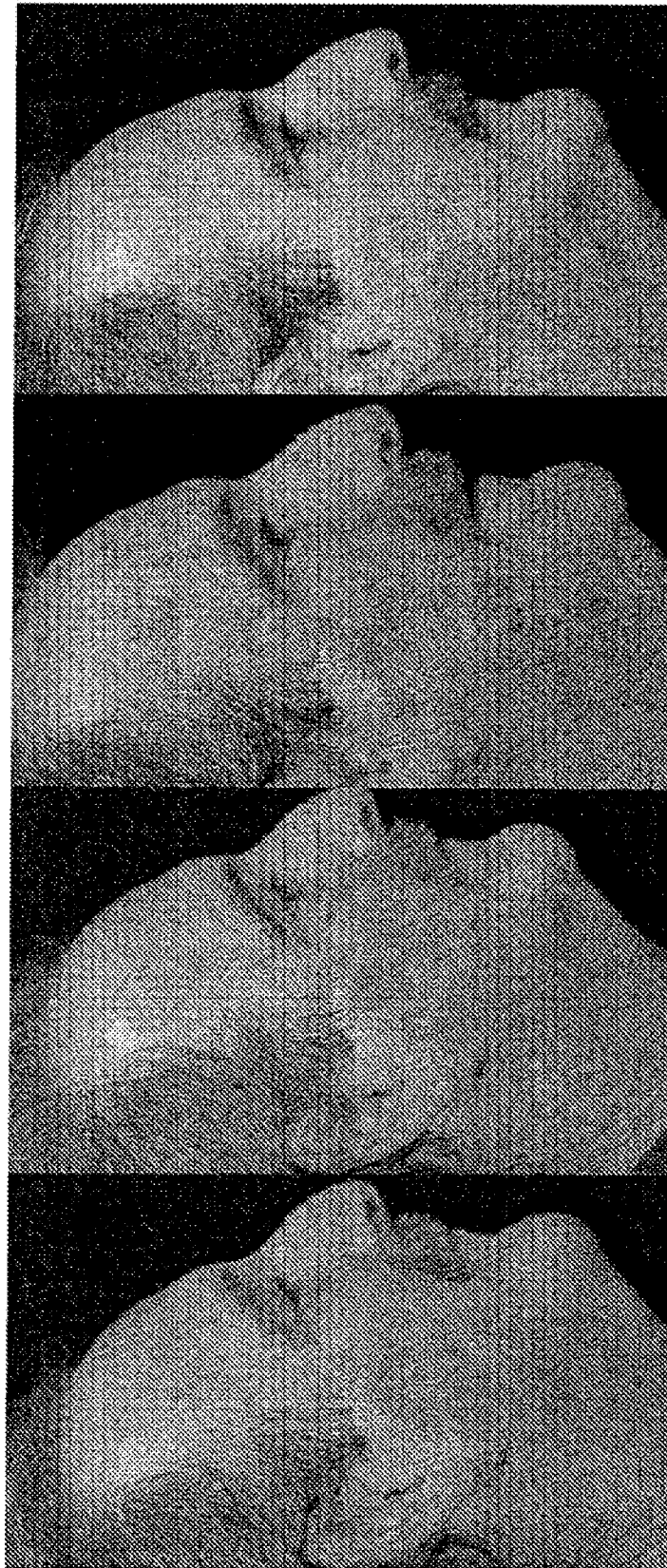
	1 min	15-60min (max)
low	35C	38C
med	36C	39C
high	37C	42C





17 minute incubation
20% ALA solution
38-42C space heater

Fig. 16



baseline
(*)

immediately post
10J/cm² 417nm
blue light (b)

3 days post
thermal PDT (u)

2 months post
thermal PDT
complete clearance (o)

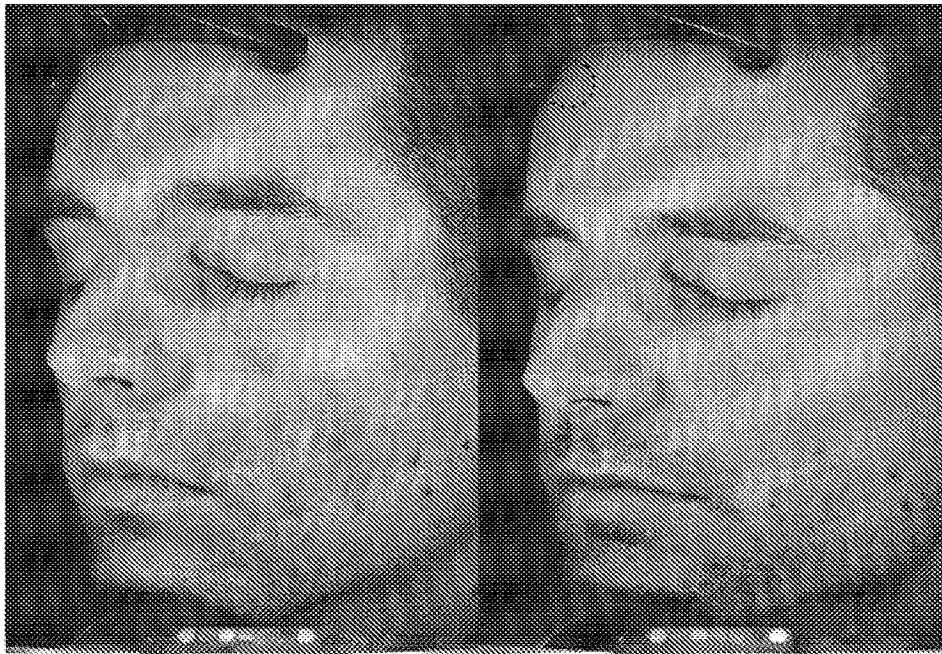


Baseline

1 month

9 months

Figure 17



Baseline

9 months

Figure 18



Figure 19

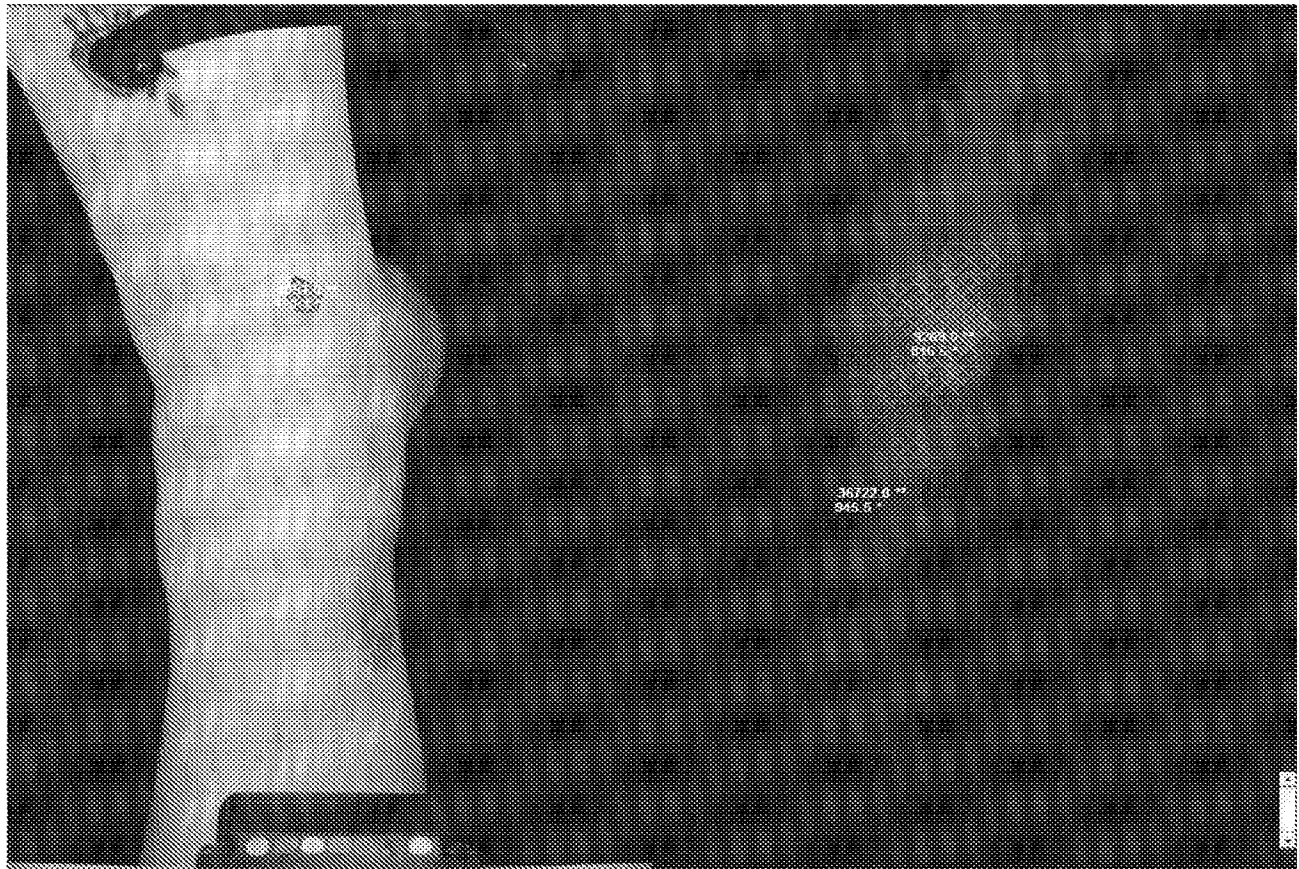


Figure 20

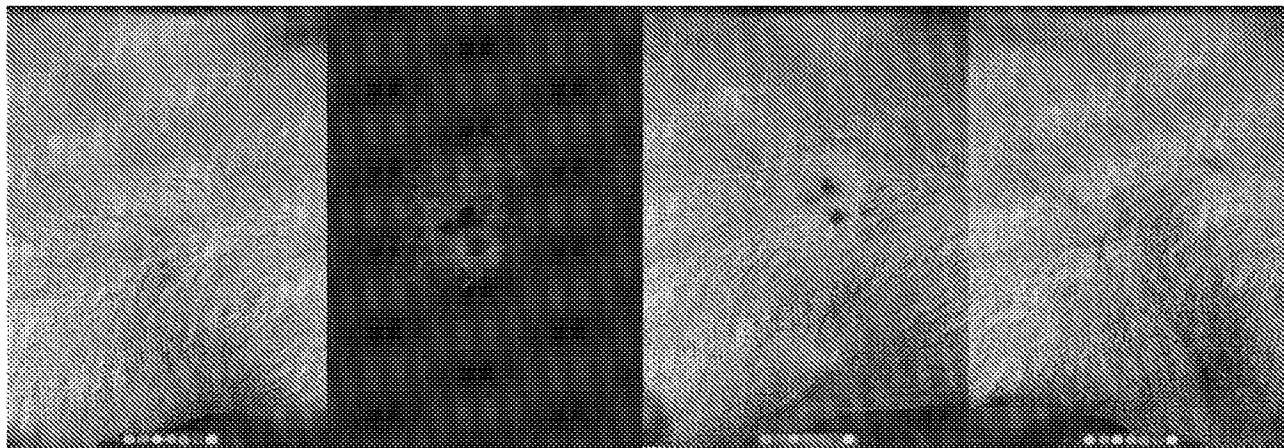
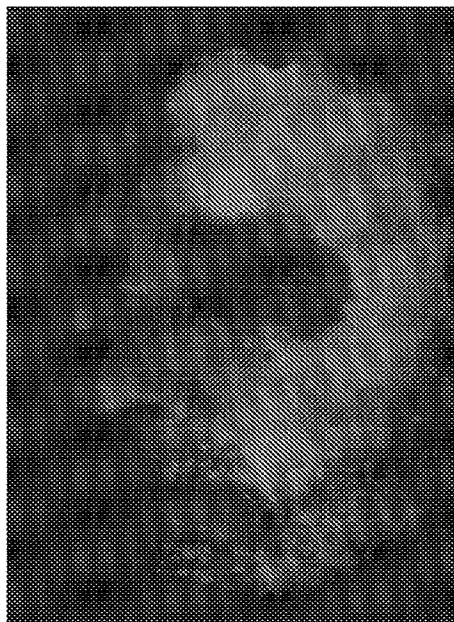
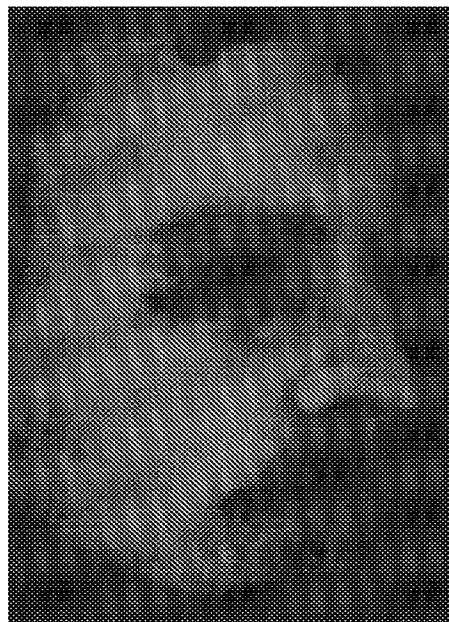


Figure 21

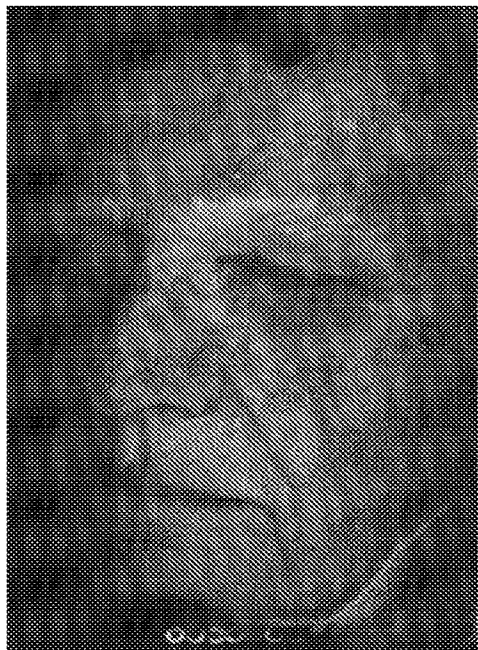


Porphyrins 3 Hours at Room Temp
(room 70F, skin 30C)



Porphyrins 30 min skin temp 40C

Figure 22



Porphyrins 1 Hour at Room Temp
(room 70F, skin 30C)



Porphyrins 30 minutes at skin temp 40C

Figure 23

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/042505

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 41/00; A61N 5/062; A61P 17/10 (2018.01)

CPC - A61K 9/0014; A61K 41/0057; A61K 41/0061; A61N 5/0616; A61N 5/062; A61N 2005/0643; A61N 2005/065; A61P 17/10 (2018.08)

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)

See Search History document

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

USPC - 514/410; 604/20; 607/88 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/0247932 A1 (BAROLET) 01 October 2009 (01.10.2009) entire document	1-4, 7, 12, 13, 16-18, 21-23, 26, 27

Y		5, 6, 8-11, 14, 15, 24, 25
Y	US 2015/0290028 A1 (ISSEROW et al) 15 October 2015 (15.10.2015) entire document	5
Y	US 2013/0274834 A1 (BAROLET et al) 17 October 2013 (17.10.2013) entire document	6, 24, 25
Y	US 2016/0008623 A1 (PHOTOCURE ASA) 14 January 2016 (14.01.2016) entire document	8, 10, 11, 14, 15
Y	US 2009/0324727 A1 (FOGUET ROCA) 31 December 2009 (31.12.2009) entire document	9
A	US 2015/0238776 A1 (THE GENERAL HOSPITAL CORPORATION D/B/A MASSACHUSETTS GENERAL HOSPITAL) 27 August 2015 (27.08.2015) entire document	1-18, 21-27
A	US 2013/0289089 A1 (MORRIS et al) 31 October 2013 (31.10.2013) entire document	1-18, 21-27
A	US 2008/0188558 A1 (GODAL et al) 07 August 2008 (07.08.2008) entire document	1-18, 21-27

☐ 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 August 2018

Date of mailing of the international search report

02 OCT 2018

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, VA 22313-1450

Facsimile No. 571-273-8300

Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300

PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2018/042505

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.: 19, 20
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.

Electronic Acknowledgement Receipt

EFS ID:	42714094
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	13-MAY-2021
Filing Date:	14-FEB-2020
Time Stamp:	12:36:38
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	Transmittal Letter	IDSTrans.pdf	113306	no	2
			bb9019aa921f00a4a7cf5cd51dd31bdd39a172cf		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	107268 42c35699ce35985dc74583b8eab2c6b4c9b a8dfd	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NPL_Barolet.pdf	2165435 4a206140cb091dd2681ba3eb8697e34081 a4a344	no	8
Warnings:					
Information:					
4	Non Patent Literature	EPSrchRpt_031221.pdf	754492 a8a9fd90a505de8f0a616f04db040dc9e35e e8f7	no	10
Warnings:					
Information:					
5	Non Patent Literature	NPL_VANDENAKKER.pdf	2464241 f352d41837cd8816deaf0ed80f508c2bbb15 06da	no	5
Warnings:					
Information:					
6	Non Patent Literature	NPL_Juzenas.pdf	1416264 62c81d8f33c8ec1d83d94dd5ff4012c11797 1203	no	4
Warnings:					
Information:					
7	Non Patent Literature	ISR_10022018.pdf	152484 94a8de50e1786592c2c448cd3c914b319ee 2dda9	no	4
Warnings:					
Information:					
8	Foreign Reference	WO_2019_018408.pdf	22143584 48e0f62d2ce4835e663bcbccca3c22ca068c 88f1	no	70
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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: CENTRAL, DOCKET
Art Unit: 3600
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents listed on the attached PTO/SB/08 were cited as being relevant in connection with a PCT and/or European application. A copy of the extended European Search Report dated March 12, 2021 is submitted herewith (document F11), as well as an International Search Report (document F14) of PCT/US2018/042505 (document F9).

Document F7 is the US counterpart of document F9.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 13, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: June 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3600
Examiner Name	CENTRAL, DOCKET				
Attorney Docket Number	067286-0410				
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)			
	G1	7,033,381-B1	04-25-2006	LARSEN, ERIK	
	G2	7,730,893-B2	06-08-2010	DOUGAL, GORDON REX PATERSON	
	G3	2019/0290763-A1	09-26-2019	LUNDAHL ET AL.	
	G4	2020/0269063-A1	08-27-2020	BOYAJIAN ET AL.	
	G5	2020/0398071-A1	12-24-2020	BOYAJIAN ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
	G6	DE-69827286-T2	11-10-2005	VIRULITE LTD [GB]		ABS
	G7	WO-93/09847-A1	05-27-1993	LARSEN ERIK [CH]		ABS

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 ⁶
	G8	BRAATHEN, LASSE R., ET AL. "Guidelines on the Use of Photodynamic Therapy for Nonmelanoma Skin Cancer: an International Consensus." Journal of the American Academy of Dermatology 56.1, January 2007, pages 125-143.	
	G9	DRAGIEVA, G. ET AL., "A Randomized Controlled Clinical Trial of Topical Photodynamic Therapy with Methyl Aminolaevulinate in the Treatment of Actinic Keratoses in Transplant Recipients." British Journal of Dermatology 151.1, July 2004, pages 196-200.	
	G10	KURWA, HABIB A., ET AL., "A Randomized Paired Comparison of Photodynamic Therapy and Topical 5-Fluorouracil in the Treatment of Actinic Keratoses." Journal of the American Academy of Dermatology 41.3, September 1999, pages 414-418.	
	G11	MACCORMACK, MOLLIE A., "Photodynamic Therapy in Dermatology: An Update on Applications and Outcomes." Seminars in Cutaneous Medicine and Surgery. Vol. 27, No. 1, WB Saunders, March 2008, pages 52-62.	
	G12	OZOG, DAVID M., ET AL., "Photodynamic Therapy: A Clinical Consensus Guide." Dermatologic Surgery 42.7, July 2016, pages 804-827.	
	G13	WOLF, PETER, ET AL., "Topical Photodynamic Therapy With Endogenous Porphyrins After Application of 5-Aminolevulinic Acid: An Alternative Treatment Modality for Solar Keratoses, Superficial Squamous Cell Carcinomas, and Basal Cell Carcinomas?" Journal of the American Academy of Dermatology 28.1, January 1993, pages 17-21.	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: June 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3600
				Examiner Name	CENTRAL, DOCKET
Sheet	2	of	2	Attorney Docket Number	067286-0410

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 ⁶
	G14	Extended European Search Report, Application No. 20214586.8, June 2, 2021, 8 pages	
	G15	USPTO Notice of Allowance, 16/438,702 (067286-0405), 05/20/2021, 10 pages	

Examiner Signature		Date Considered	
-------------------------------	--	----------------------------	--



Espacenet

Bibliographic data: DE69827286 (T2) — 2005-11-10

ELECTROMAGNETIC RADIATION THERAPY

Inventor(s): DOUGAL REX [GB] ± (DOUGAL, REX)

Applicant(s): VIRULITE LTD [GB] ± (VIRULITE LTD., DARLINGTON)

Classification: - **international:** A61N5/06; (IPC1-7): A61N5/06
 - **cooperative:** A61N5/06 (EP); A61N5/0616 (EP); A61N2005/0642 (EP); A61N2005/0644 (EP); A61N2005/0645 (EP); A61N2005/0652 (EP)

Application number: DE1998627286T 19981012

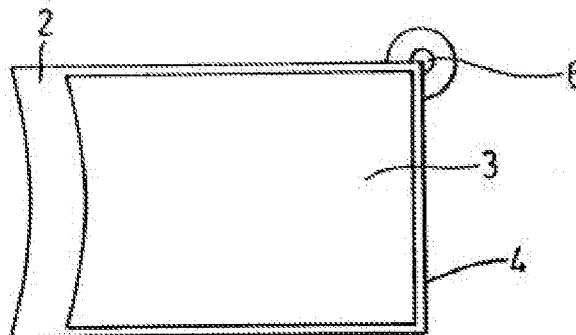
Priority number(s): WO1998GB03073 19981012 ; GB19970021506 19971010 ; GB19970027441 19971231

Also published as: AT280619 (T) AU737699 (B2) AU9547498 (A) CA2304774 (A1) CA2304774 (C) DK1021223 (T3) EP1021223 (A1) EP1021223 (B1) ES2230718 (T3) GB2344532 (A) GB2344532 (B) JP2001519217 (A) JP2009106764 (A) JP4257718 (B2) PT1021223 (E) US2005234383 (A1) US2007129778 (A1) US7730893 (B2) WO9919024 (A1) less

Abstract not available for DE69827286 (T2)

Abstract of corresponding document: WO9919024 (A1)

An electromagnetic radiation therapy system comprises means for emitting divergent electromagnetic radiation having a wavelength between 950 and 1500 nm and being capable of producing, at the site being treated, a radiation intensity of at least 50 mW/cm². Also disclosed are the use of the system for treating various conditions and the method of applying the treatment.





(19)
Bundesrepublik Deutschland
Deutsches Patent- und Markenamt

(10) **DE 698 27 286 T2 2005.11.10**

(12)

Übersetzung der europäischen Patentschrift

(97) **EP 1 021 223 B1**

(51) Int Cl.⁷: **A61N 5/06**

(21) Deutsches Aktenzeichen: **698 27 286.2**

(86) PCT-Aktenzeichen: **PCT/GB98/03073**

(96) Europäisches Aktenzeichen: **98 949 091.7**

(87) PCT-Veröffentlichungs-Nr.: **WO 99/019024**

(86) PCT-Anmeldetag: **12.10.1998**

(87) Veröffentlichungstag
der PCT-Anmeldung: **22.04.1999**

(97) Erstveröffentlichung durch das EPA: **26.07.2000**

(97) Veröffentlichungstag
der Patenterteilung beim EPA: **27.10.2004**

(47) Veröffentlichungstag im Patentblatt: **10.11.2005**

(30) Unionspriorität:

9721506	10.10.1997	GB
9727441	31.12.1997	GB

(84) Benannte Vertragsstaaten:

**AT, BE, CH, CY, DE, DK, ES, FI, FR, GR, IE, IT, LI,
LU, MC, NL, PT, SE**

(73) Patentinhaber:

Virulite Ltd., Darlington, GB

(72) Erfinder:

DOUGAL, Rex, Gordon, Hartlepool TS24 9AH, GB

(74) Vertreter:

Freischem und Kollegen, 50667 Köln

(54) Bezeichnung: **ELEKTROMAGNETISCHE BESTRAHLUNGSTHERAPIE**

Anmerkung: Innerhalb von neun Monaten nach der Bekanntmachung des Hinweises auf die Erteilung des europäischen Patents kann jedermann beim Europäischen Patentamt gegen das erteilte europäische Patent Einspruch einlegen. Der Einspruch ist schriftlich einzureichen und zu begründen. Er gilt erst als eingelegt, wenn die Einspruchsgebühr entrichtet worden ist (Art. 99 (1) Europäisches Patentübereinkommen).

Die Übersetzung ist gemäß Artikel II § 3 Abs. 1 IntPatÜG 1991 vom Patentinhaber eingereicht worden. Sie wurde vom Deutschen Patent- und Markenamt inhaltlich nicht geprüft.

Beschreibung

Gebiet der Erfindung

[0001] Diese Erfindung bezieht sich auf eine Vorrichtung zur Erzeugung elektromagnetischer Strahlung für die Behandlung von Krankheiten und für den Erhalt oder die Verbesserung von Organen oder Körpergeweben, einschließlich Muskeln. Diese Erfindung kann in Verbindung mit der Heilung oder Linderung einer Vielfalt von Krankheiten einschließlich Infektionskrankheiten und pathologischer Prozesse verwendet werden, insbesondere solcher, die von Viren und Bakterien verursacht wurden.

[0002] Beispielhaft kann die Erfindung in Verbindung mit Krankheiten verwendet werden, die durch das Herpes-Virus verursacht werden, von dem bekannt ist, daß es für eine Vielzahl von üblichen Beschwerden, umfassend korneale dendritische Geschwüre, Genitalherpes, Herpes Labialis (Fieberbläschen), Herpes zoster (Gürtelrose) und Herpes stomatitis verantwortlich ist. Diese Infektionen tendieren dazu, immer wiederzukehren und werden von bestehenden, medizinisch akzeptierten Behandlungen nicht geheilt.

Hintergrund der Erfindung

[0003] Gegenwärtig medizinisch akzeptierte Verfahren zur Behandlung von Infektionen, die durch das Herpes-Virus verursacht werden, sind Chemotherapeutika, die topisch verabreicht, injiziert oder oral eingenommen werden. Eine derartige Behandlung kann oft die unmittelbare Infektion bewältigen, jedoch verhindert sie eine Wiederkehr der Infektion zu einem späteren Zeitpunkt nach Einstellung der Behandlung nicht.

[0004] Es ist seit einigen Jahrzehnten bekannt, daß die Verwendung von Licht einen positiven therapeutischen Effekt bei der Behandlung eines breiten Spektrums von Krankheiten bewirken kann. In den 1960er Jahren wurde die Verwendung von Licht schmalbandiger Wellenlängen in in vivo/in vitro Experimenten untersucht. Es wurde festgestellt, daß Licht mit Wellenlängen größer als 440 nm nicht wirkt. Weitere Untersuchungen wurden mit Licht, das eine Wellenlänge von 300 bis 350 nm (UV-Licht) aufwies, durchgeführt, aber es wurde entdeckt, daß die Infektion sich eher verschlimmerte/gefördert wurde, als daß sie sich besserte/beseitigt wurde. Einige Versuche wurden unternommen, um mit dem Herpes-Virus befallene Personen durch die Behandlung mit Licht mit einer Wellenlänge von 660 nm zu behandeln, wie in US 5500009 beschrieben. Jedoch war es dem gegenwärtigen Erfinder nicht möglich, ein signifikantes klinisches Ergebnis oder einen Vorteil bei dieser Wellenlänge zu erzielen.

[0005] Zusätzlich ist es aus dem Stand der Technik bekannt, einen Laser zu verwenden, um kohärente Strahlung zu erzeugen und diese auf den zu behandelnden Bereich zu fokussieren. Eine Behandlung mit einem Nd-YAG-Laser mit einer Basis-Wellenlänge von 1064 nm ist mit verringerten Schmerzen, einer verringerten Narbenbildung und einer verbesserten Heilung verbunden (US 5445146). Zusätzlich wurde berichtet, daß Dioden, welche Licht mit der roten Wellenlänge von 940 ± 25 nm emittieren, verwendet werden können, um eine Auswahl von wesentlichen Skelettmuskel-Beschwerden zu behandeln (US 5259380). Jedoch gibt es keine Anzeichen, daß Licht mit einer Wellenlänge über dieser von irgendeinem therapeutischen Nutzen sein kann. EP 0416150 offenbart ein elektromagnetisches Therapiesystem, wie im Oberbegriff des Anspruchs 1 definiert. Eine Wellenlänge im Bereich zwischen 600 nm und 1100 nm wird für die Bio-Stimulation und die Herpes-simplex-Behandlung vorgeschlagen.

[0006] Es wurde nun überraschenderweise festgestellt, daß elektromagnetische Strahlung mit geringer Intensität und kleiner Bandbreite wirksam ist bei der Behandlung von Infektionskrankheiten, Entzündungs-Krankheitstypen und anderen Zuständen, einschließlich der Schmerzlinderung. Es ist postuliert, daß die Art und Weise, in der die elektromagnetische Strahlung ihre Wirkung herbeiführt, durch Energieübertragung durch zelluläre Komponenten/Organeln gegeben ist.

[0007] Ein Wassermolekül, das einen Bereich von es durchsetzenden elektromagnetischen Strahlungswellenlängen aufweist, wird mehrere Transmissions-Peaks erzeugen. Diese Transmissions-Peaks sind dem für die Erfindung bevorzugten Wellenlängenbereich der therapeutischen elektromagnetischen Strahlung zugeordnet und implizieren daher eine Funktion des Wassermoleküls in dem allgemeinen Wirkungsmechanismus.

Darlegung der Erfindung

[0008] Gemäß der vorliegenden Erfindung wird ein System zur Therapie mit elektromagnetischer Strahlung bereitgestellt, mit einem Mittel zur Emission schmalbandiger divergenter elektromagnetischer Strahlung und

welches geeignet ist, an der Behandlungsstelle eine Strahlungsintensität von mindestens 50 $\mu\text{Watt}/\text{cm}^2$ und bis zu 2 Watt/cm^2 zu erzeugen, dadurch gekennzeichnet, daß die Wellenlänge der elektromagnetischen Strahlung 1072 nm oder 1268 nm beträgt.

[0009] Der Bezug hierin auf die Behandlungsstelle ist, ohne Einschränkung, dazu bestimmt, die Haut oder Muskulatur oder ein inneres Organ eines Menschen oder eines Tieres zu umfassen.

[0010] Unsere Studien haben gezeigt, daß eine Wellenlänge von 1072 nm, insbesondere bei der Behandlung von herpetischen und bakteriellen Infektionen, der Linderung akuter Schmerzen und bei der Behandlung von Augenzuständen effektiv ist, während eine Wellenlänge von 1268 nm insbesondere effektiv ist, um für eine Schmerzlinderung bei tiefen Muskelverletzungen zu sorgen. Es ist zu bemerken, daß diese beiden bevorzugten Wellenlängen den Peak-Emissionswellenlängen des Licht-Transmissionsprofils eines Wassermoleküls entsprechen, und daher nehmen wir an, daß der Wirkungsmechanismus mit Wasser und möglicherweise mit Zellmembranen in Zusammenhang steht.

[0011] Mit divergent ist gemeint, daß die elektromagnetische Strahlung, die von dem System der Erfindung emittiert wird, einen halben Divergenzwinkel von mindestens 5° aufweist. Vorzugsweise liegt die Divergenz der elektromagnetischen Strahlung hinsichtlich des halben Divergenzwinkels im Bereich von 15° bis 45° .

[0012] Vorzugsweise ist die elektromagnetische Strahlung kontinuierlich oder gepulst.

[0013] Vorzugsweise beträgt die Intensität für die Behandlung von Augen und Schleimhäuten bei einer kontinuierlichen elektromagnetischen Strahlung mindestens 50 $\mu\text{Watt}/\text{cm}^2$ und bis 2 Watt/cm^2 , sowie mindestens 500 $\mu\text{Watt}/\text{cm}^2$ und bis 2 Watt/cm^2 für die Hautbehandlung.

[0014] Vorzugsweise beträgt die Spitzenintensität (Peakintensität) für die Behandlung von Augen und Schleimhäuten bei einer gepulsten elektromagnetischen Strahlung mindestens 50 $\mu\text{Watt}/\text{cm}^2$, und bevorzugter beträgt die Spitzenintensität (Peakintensität) für die Hautbehandlung mindestens 500 $\mu\text{Watt}/\text{cm}^2$, und die durchschnittliche Intensität beträgt bis zu 2 Watt/cm^2 . Die mittlere Intensität ist die Spitzenintensität (Peakintensität) multipliziert mit dem Anteil der Gesamtzeit, in der die Strahlung angewandt wird. Beispielsweise beträgt die mittlere Intensität 30 $\mu\text{Watt}/\text{cm}^2$, wenn die Spitzenintensität (Peakintensität) 500 $\mu\text{Watt}/\text{cm}^2$ beträgt und für 10 $\mu\text{Sekunden}$ mit einer Frequenz von 600 Hz gepulst wird.

[0015] Vorzugsweise liegt die mittlere Intensität bei einer gepulsten elektromagnetischen Strahlung im Bereich von 50–100 $\mu\text{Watt}/\text{cm}^2$.

[0016] Wir haben festgestellt, daß die Intensität geeigneter Weise von einer Spitzenintensität (Peakintensität) von 500 $\mu\text{Watt}/\text{cm}^2$ bis zu einer kontinuierlichen Intensität oder Spitzenintensität (Peakintensität) von 2 Watt/cm^2 reichen kann, wenn sie auf die Haut aufgebracht wird. Im Falle der Anwendung elektromagnetischer Strahlungstherapie bei einem Auge oder der Schleimhaut haben sich so geringe kontinuierliche oder gepulste Intensitäten wie 50 $\mu\text{Watt}/\text{cm}^2$ als vorteilhaft erwiesen. Typischerweise werden 10 mWatt/cm^2 auf der Haut verwendet, doch dieser Wert hängt davon ab, wie fett oder muskulös das Subjekt ist und daher wie tief das zu behandelnde Gewebe/Gebiet/Organ unter der Hautoberfläche liegen kann. Typischerweise wird auf Schleimhäuten eine Strahlung mit der Intensität von 5 mWatt/cm^2 angewendet.

[0017] Vorzugsweise wird bei einer gepulsten elektromagnetischen Strahlung diese für Zeitdauern von mindestens 10–15 $\mu\text{Sekunden}$ angewendet, und bevorzugter wird sie bei einer Frequenz/Wiederholungsrate im Bereich von 480–800 Hz angewendet, wobei die Frequenz/Wiederholungsrate bei oder ca. bei 600 Hz bevorzugter ist.

[0018] Unsere Studien haben gezeigt, daß die elektromagnetische Strahlung entweder kohärent oder nicht kohärent sein kann, wobei die klinischen Ergebnisse durch diesen Parameter nicht beeinflußt werden.

[0019] Vorzugsweise wird die elektromagnetische Strahlung auf den betroffenen Bereich für mindestens 30 Sekunden und bis zu einigen Minuten aufgebracht. Eine typische Einwirkungsdauer für die Haut oder das Auge liegt im Bereich von 3 Minuten, jedoch wird diese Zeit für Gewebe deutlich unterhalb der Hautoberfläche gemäß der Fett-/Muskelschicht-Tiefe der Personen erhöht, und die Einwirkung kann bis zu 10 Minuten betragen.

[0020] Es sollte gewürdigt werden, daß die Energiequelle, welche die elektromagnetische Strahlung emittiert, mehr als die für den klinischen Effekt erforderliche Intensität erzeugen muß, da wir gezeigt haben, daß ca. 99%

der aufgetragenen therapeutischen Lichtmenge während der Behandlung über der Hautoberfläche verloren geht. Daher ist die Intensität der aufgetragenen Strahlung bei der Durchführung einer Behandlung zu korrigieren.

[0021] Unsere Studien haben ergeben, daß für herpetische Infektionen erste klinische Effekte nach einer Behandlung von 30 Sekunden nachgewiesen werden können und daß der Hauptanteil unmittelbarer klinischer Effekte nach einer Behandlung von 90 Sekunden wahrgenommen wird. Jedoch sind bestimmte Gewebe empfindlicher, so daß beispielsweise die Schleimhäute dem dosierenden System für ca. 30 Sekunden ausgesetzt werden, und unmittelbare klinische Effekte werden bereits nur nach 3 Sekunden Behandlung bemerkt.

[0022] Aus dem Vorhergehenden ist ersichtlich, daß die elektromagnetische Strahlung zu dem Zielort gelenkt werden kann, entweder auf eine kontinuierliche oder geschaltete (gepulste) Art und Weise. Der Hauptvorteil des Schaltens besteht darin, daß es Energieeinsparung und den Anlagen eine viel höhere Spitzenintensitäts (Peakintensitäts)-Ausgabe ermöglicht, wodurch die klinische Wirkung erhöht wird.

[0023] Vorzugsweise enthält das System zur Therapie mit elektromagnetischer Strahlung auch ein Mittel zur Verringerung des Betrages der Umgebungsstrahlung, der auf die Infektionsstelle auftritt. Die Anwesenheit von ultraviolettem Licht und violettem Licht, wie im Sonnenlicht, verschlimmert die herpetischen Zustände, und es ist bevorzugt, Wellenlängen unterhalb von 400 nm auszuschließen. Noch bevorzugter ist es, wenn Wellenlängen unterhalb von 500 nm ausgeschlossen sind.

[0024] Vorzugsweise enthält das System ferner Mittel, um die Intensität der Strahlung innerhalb eines vorbestimmten Bereichs zu halten. Die ausgegebene Strahlung kann mit einer sichtbaren Anzeige überwacht werden, welche die fehlerfreie Wirkungsweise der Vorrichtung sowohl hinsichtlich der Intensität als auch hinsichtlich der Wellenlänge anzeigt.

[0025] Vorzugsweise enthält das System ferner ein Mittel zur Steuerung/Regelung der Anwendungsdauer der Strahlung. Demnach betrifft die vorliegende Erfindung die Verwendung von elektromagnetischer Strahlung, welche eine Wellenlänge in einem Bereich vom Sichtbaren in das Infrarote aufweist und welche mit einer derartigen geringen Intensität aufgebracht wird, so daß keine thermische Beschädigung an irgendeinem humanen oder tierischem Gewebe verursacht wird.

[0026] In dem Fall, wo das System auf eine Art und Weise verwendet wird, daß die Strahlung dazu veranlaßt wird, in das Auge einzudringen, ist es bevorzugt, daß die Intensität 100 mWatt/cm² nicht überschreitet. Andererseits kann die Intensität höher sein und kann geeignet in gepulster Form abgegeben werden, wodurch man mehrere Watt momentaner Ausgangsleistung erhält, die ein gutes Durchdringen des Gewebes und einen wesentlichen systemischen Effekt ermöglicht.

[0027] Das Mittel zur Erzeugung der Strahlung ist vorzugsweise eine Licht emittierende Festkörpervorrichtungen, bevorzugter eine Licht emittierende Festkörperdiode oder eine Gasentladungs-Vorrichtungen. Die Strahlung derartiger Vorrichtungen kann elektrisch betrieben werden, oder die Strahlung kann über ein faser-optisches Zuführungssystem zu einem Applikator geführt werden.

[0028] Vorzugsweise enthält der Strahlungs-Emitter einen PN-Übergang, der dazu ausgebildet ist, die Strahlung mit einer Wellenlänge von 1072 nm oder 1268 nm zu emittieren. Eine einzelne Leuchtdioden-Anordnung kann eine Vielzahl von orientierten Übergängen enthalten.

[0029] Infrarot emittierende Dioden können nicht nur angeordnet werden, um Strahlung bei einer bestimmten Frequenz zu emittieren, sondern auch um einen divergenten Strahl mit hoher Intensität zu emittieren.

[0030] Eine Gasentladungs-Vorrichtung kann eine Mischung von Gasen enthalten, die eine Ausgabe bei der gewünschten Wellenlänge von beispielsweise 1072 nm herbeiführt.

[0031] Die Vorrichtung gemäß der vorliegenden Erfindung kann dafür verwendet werden, einen Bereich des biologischen Gewebes eines lebenden Menschen oder Tieres zu behandeln, indem eine divergente elektromagnetische Strahlung, welche eine Wellenlänge von 1072 nm oder 1268 nm und eine Intensität von mindestens 50 µWatt/cm² und bis zu 2 Watt/cm² aufweist, verwendet wird.

[0032] Vorzugsweise wird die elektromagnetische Strahlung, wie sie durch das System der Erfindung erzeugt wird, bereitgestellt für die Behandlung von Zuständen, wie etwa, aber nicht eingeschränkt auf, herpetische In-

fektionen, bakterielle und/oder Virus-Infektionen der Haut oder der oberen Atemwege, Augenkrankheitszustände, wie das "Trockene Augen-Syndrom", brennende Verletzungen, Skelettmuskel-Zustände, Entzündungszustände, wie der rheumatischen Arthritis und bösartigen Tumoren, zur Reduktion der Narbenbildung, der Förderung der Wundheilung, der sportlichen Leistung und der Schaffung akuter und chronischer Schmerzbefreiung.

[0033] Die Verwendung einer Strahlung mit eingeschränkter Bandbreite kann das Immunsystem stärken, mit dem Ergebnis, daß es dem Körper möglich ist, Infektionen wie das Herpes-Virus zu bekämpfen.

[0034] Obwohl auf Infektionen, die durch das Herpes-Virus verursacht wurden, Bezug genommen wurde, ist die vorliegende Erfindung nicht auf derartige Infektionen beschränkt. Sie ist bei anderen Infektionen anwendbar, die von allen Viren verursacht werden, einschließlich HIV, den gewöhnlichen Erkältungs- und Influenza-Viren.

[0035] Das Verfahren der Behandlung eines Bereiches des biologischen Gewebes eines lebenden Menschen oder eines Tieres umfaßt den Schritt des Aufbringens divergenter elektromagnetischer Strahlung auf den genannten Bereich, welche eine Wellenlänge zwischen 950 nm und 1500 nm bei einer Intensität von mindestens 50 $\mu\text{Watt}/\text{cm}^2$ aufweist.

[0036] Vorzugsweise wird der zu behandelnde Bereich so angestrahlt, daß das betroffene Gewebe in Abhängigkeit von dem zu behandelnden Gewebe eine Strahlungsenergie von mindestens 50–500 $\mu\text{Watt}/\text{cm}^2$ Spitzenintensität (Peakintensität) erhält. Ein vorliegender Faktor ist die Bestrahlungs-Dauer und vorzugsweise sollte die Dauer mindestens ein spezifiziertes Minimum von 10–15 $\mu\text{Sekunden}$ bei einer Wiederholungsrate/Frequenz von 450–800 Hz betragen, und vorzugsweise für eine Dauer von mindestens 30 Sekunden.

Kurze Beschreibung der Zeichnungen

[0037] Ausführungsformen der Erfindung werden nun, jedoch nur beispielhaft und in Bezug auf die beigefügten Zeichnungen, beschrieben, in denen:

[0038] Fig. 1 bis Fig. 4 eine Ansicht mit entfernter Abdeckung, eine Seitenansicht, eine Unteransicht bzw. eine Vorderansicht einer ersten Ausführungsform gemäß der vorliegenden Erfindung zeigen;

[0039] Fig. 5 bis Fig. 7 eine Vorderansicht, eine Draufsicht und eine Unteransicht einer zweiten Ausführungsform gemäß der vorliegenden Erfindung zeigen;

[0040] Fig. 8 bis Fig. 10 eine Hinteransicht, eine Draufsicht und eine Seitenansicht einer dritten Ausführungsform der vorliegenden Erfindung zeigen;

[0041] Fig. 11 und Fig. 12 eine Seitenansicht und eine Ansicht von rechts (wie in Fig. 11 zu sehen) einer vierten Ausführungsform gemäß der vorliegenden Erfindung zeigen; und

[0042] Fig. 13 und Fig. 14 weitere Ausführungsformen der vorliegenden Erfindung zeigen.

Detaillierte Beschreibung der bevorzugten Ausführungsformen

[0043] Bezugnehmend auf die Fig. 1 bis Fig. 4, enthält eine erste Ausführungsform gemäß der vorliegenden Erfindung eine tragbare divergente Strahlungsquelle **4** mit einem eingebauten Zeitgeber und einem Umgebungs-Strahlungsdetektor. Eine einzelne Wellenlänge wird zu einer beliebigen Zeit verwendet. Die effektiven Wellenlängen sind 1072 nm und 1268 nm.

[0044] Bei einer anderen Ausführungsform der vorliegenden Erfindung werden zwei Wellenlängen verwendet, wobei eine sichtbar und die andere unsichtbar ist, insbesondere in dem Fall, in dem die optimale Wellenlänge im Infraroten liegt.

[0045] Die Strahlungsquelle **4** enthält einen länglichen Hohlkörper mit rechteckigem Querschnitt mit einem Ende **8**, welches lichtdurchlässig ist. Die Strahlungsquelle enthält eine Anordnung von Licht emittierenden Dioden **2**, die nahe zu dem lichtdurchlässigen Ende **8** angeordnet sind. Die Energie wird von Batterien, die im Hohlraum **3** des Körpers **4** angeordnet sind, zu den Vorrichtungen **2** übertragen.

[0046] Die Strahlungsquelle ist mit zwei An/Aus-Schaltern **5** versehen, die betätigt werden können, um den Betrieb der internen Elektronik auszulösen. Beide Schalter sind gleichzeitig zu drücken, um die Vorrichtung korrekt zu betreiben, wodurch eine versehentliche Verwendung der Vorrichtung vermieden wird. Nahe dem dem lichtdurchlässigen Ende **8** gegenüberliegenden Ende befindet sich ein Nutz-Loch **6**, das es ermöglicht, die Strahlungsquelle aufzuhängen oder andere Artikel, wie einen Schlüsselbund, anzubringen.

[0047] Die Strahlungsquelle ist mit einer Steuer-/Regel-Elektronik versehen, welche die Zeit, in der die Strahlungsquelle eingeschaltet ist, begrenzt und dann die Strahlungsquelle automatisch ausschaltet. Die Steuer-/Regelektronik überwacht die Umgebungsstrahlung, und in dem Falle, daß die Umgebungsstrahlung eine Intensität aufweist, die den therapeutischen Effekt der Strahlungsquelle stört, tönt ein Alarmsummer (nicht dargestellt). Die Strahlungsemissions-Vorrichtungen **2** und ihre Position und Anordnung innerhalb der Strahlungsquelle sind derart, daß die von der Strahlungsquelle emittierte Strahlung die Form eines divergenten Lichtstrahls aufweist. Die Kante **1** schränkt während der Behandlung die auf den Bereich einfallende Umgebungsstrahlung ein.

[0048] Das Strahlungstherapie-System der vorliegenden Erfindung kann dazu ausgebildet sein, transportierbar zu sein und von solchen Personen verwendet zu werden, die ihre eigenen, eigenständigen und batteriebetriebenen Vorrichtungen wünschen. Zusätzlich kann es derart ausgebildet sein, daß während der Verwendung ein tierisches oder ein menschliches Appendix innerhalb eines Hohlkörpers **3** angeordnet werden kann, um die von diesem emittierte Strahlung zu erhalten. Diese besondere Modifikation ist insbesondere für die Behandlung von Genitalherpes um den Hodensack und/oder Penis herum geeignet.

[0049] Bezugnehmend auf Fig. 5 bis Fig. 7 der beigefügten Zeichnung ist eine zweite Ausführungsform gemäß der vorliegenden Erfindung in der Form einer Viel-Platten-Strahlungsquelle ausgebildet. In diesem Fall ist eine Vielzahl von Platten A nebeneinander an Drehgelenken **7** und **7A** befestigt, die wiederum mittels Armen **8** und **10** mit einer Stütze **9** verbunden sind. Die Anordnung ist derart, daß sich die Platten relativ zueinander bewegen können, und die Stütze kann eingestellt werden, um die Strahlungsrichtung zu ändern. Der Ständer erstreckt sich entweder vom Boden oder ist an einem Stuhl oder einem Bett angebracht.

[0050] Die Vorderwand einer jeden Platte A ist lichtdurchlässig, und unterhalb der Vorderwand ist eine Anordnung von strahlungsemittierenden Vorrichtungen **2** befestigt.

[0051] Wie bei den früher oben beschriebenen Ausführungsformen enthält diese Ausführungsform der Erfindung Steuer-/Regelektroniken, um die Anwendungszeit der Strahlung zu begrenzen und die Umgebungsstrahlung zu überwachen, und stellt einen Alarm zur Verfügung, wenn der Grenzwert der Umgebungsstrahlung überschritten ist.

[0052] Die Kante **1** schließt Umgebungslicht aus, falls sich die Vorrichtung in Kontakt zu einem Körper befindet.

[0053] Bezugnehmend auf die Fig. 8 bis Fig. 10 der Zeichnungen weist eine dritte Ausführungsform gemäß der vorliegenden Erfindung die Form einer Strahlungsquelle mit einstellbarer Kopfbedeckung auf.

[0054] Die Strahlungsquelle ist bei Verwendung mittels eines Bandes oder eines Helms B auf dem Kopf des Bedieners angeordnet und enthält zwei Platten **11A** und **11B** von Strahlungsemissions-Vorrichtungen, wobei die Platten **11A** und **11B** mittels einer Zwischenaussparung **13** voneinander getrennt sind. Diese Strahlungsplatten **11A** und **11B** können entweder gleichzeitig oder getrennt voneinander verwendet werden, wobei dort ein Schalter (nicht dargestellt) bereitgestellt ist, um die elektrische Energie zu einer oder beiden Platten zu lenken. Die Strahlungsplatten **11A** und **11B** werden durch einstellbare Steuer-/Regelelemente **12** und **12A** nahe den Augen gehalten.

[0055] Die Strahlungsquelle ist mit einer Steuer-/Regelektronik **4** versehen, die die Anwendungszeit der Photonen auf die betroffene Stelle begrenzt und die Strahlung am Ende der Anwendungsdauer automatisch ausschaltet. Wie zuvor überwacht die Steuer-/Regelektronik die Umgebungsstrahlung und stellt einen Alarm zur Verfügung, wenn der Grenzwert überschritten ist.

[0056] Bezugnehmend auf die Fig. 11 und Fig. 12 der beigefügten Zeichnungen weist eine vierte Ausführungsform gemäß der vorliegenden Erfindung die Form einer Strahlungsquelle zur Zuführung von Photonen zu einer Öffnung auf. In diesem Fall enthält der Strahlungsquellenkörper einen länglichen zylindrischen Abschnitt **15**, der an einem Ende einen Flansch **16** aufweist, dessen Form in Fig. 12 dargestellt ist. An seinem

anderen Ende ist der längliche Abschnitt **15** halbkugelförmig (**15A**). Strahlungsemissions-Vorrichtungen sind sowohl in dem länglichen Abschnitt **15** als auch in dem Flansch **16** angeordnet, und diese Strahlungsquelle kann verwendet werden, um Photonen jeder beliebigen Öffnung des menschlichen/tierischen Körpers zuzuführen, beispielsweise in die Vagina, den After, die Mundhöhle, den Nasenrachenraum und die Wangenöffnung. Die Strahlungsquelle kann gemäß der Größe der Öffnung, in die sie einzuführen ist, in unterschiedlichen Größen bereitgestellt sein.

[0057] Die Steuer-/Regelelektronik begrenzt die Bestrahlungszeit und überwacht die Umgebungsstrahlung, wie bei den zuvor beschriebenen Ausführungsformen der Erfindung.

[0058] Fig. 13 und Fig. 14 veranschaulichen Vorrichtungen, die für die Behandlung einer gewöhnlichen Erkältung und Akne brauchbar sind.

[0059] Die gewöhnliche Erkältung wird durch eine Virus-Infektion der oberen Atemwege verursacht. Die Virus-Partikel sind nahezu ausschließlich im Rachen, den Nasennebenhöhlen und in Nasengängen vorzufinden.

[0060] Die Vorrichtung ist eine Strahlungsemissions-Vorrichtung, die eine Strahlung mit einer Wellenlänge zuführt, welche die oberflächliche Haut und das darunterliegende Gewebe in hinreichendem Ausmaß durchdringt, um einen therapeutischen Effekt zu erzeugen.

[0061] Die Vorrichtung in Fig. 14 ist anpassungsfähig und wird an dem Gesicht des Patienten angeordnet, während er auf dem Rücken liegt. Die Aussparung **18** stellt eine Öffnung für die Augen des Patienten zur Verfügung. Eine Platte A ermöglicht die Behandlung der Stirnhöhlen. Eine Platte A' ermöglicht die Behandlung der Kieferhöhlen und der Nase, und die Zwischenbrücke **17** ermöglicht die Behandlung der Siebbeinzellen und der Nase.

[0062] Die Vorrichtung in Fig. 13 ist eine anpassungsfähige Strahlungsemissions-Vorrichtung, die am Hals des Patienten angeordnet wird, so daß sich die Punkte **20** der Basis der Ohren des Patienten annähern. Diese Vorrichtung führt für den therapeutischen Effekt dem Kehlkopf, dem Mundrachenraum und dem Kehlkopfraum des Patienten Strahlung zu. Die Senke **19** paßt unter das Kinn des Patienten.

[0063] Vorrichtungen zur Behandlung von Akne sind wie in den Fig. 13 und Fig. 14 ausgebildet und weisen mehrere Platten variabler Form und Größe auf. Alle Platten weisen Strahlungsemissions-Vorrichtungen **2** auf und sind anpassungsfähig, um der Platte zu ermöglichen, der Kontur des Gesichtes und des Halses zu folgen. Die Platten A und A' (Fig. 13) werden an der unteren Seite des Kinns bzw. des Halses angebracht. Die Platten A und A' in der Vorrichtung in Fig. 14 werden an dem Gesicht angebracht, so daß die Aussparung **18** dem Patienten ermöglicht, während der Behandlung zu sehen. Die Brücke **17** behandelt den Nasenrücken und die Ausdehnung **23** die Wangen. Die Aussparung **21** liegt auf der Nasenspitze, wodurch dem Patienten ermöglicht wird, während der Behandlung bequem zu atmen. Die Platte A' wird zur Behandlung des Kinnbereichs bei Aussparung **22** und zur Behandlung des an den Mund angrenzenden Bereichs verwendet.

[0064] Bei Einbeziehung des Brustkorbs und/oder Rückens wird eine größere Version der Platte A als die in Fig. 5 verwendet.

[0065] Auf Grund der Oberflächennatur der Pathologie ist die Umgebungsstrahlung von Signifikanz, und ein Umgebungsstrahlungs-Detektor wird verwendet.

[0066] Die Behandlungszeit beträgt maximal 10 Minuten, jedoch typischerweise 5 Minuten.

[0067] Es sollte gewürdigt werden, daß zwei oder mehrere der oben beschriebenen Vorrichtungen in Verbindung zueinander verwendet werden können. Ein Beispiel ist die Behandlung der pädiatrischen herpetischen Entzündung der Mundschleimhaut, wo die Vorrichtung zur Zuführung von Strahlung zu einer Öffnung in Verbindung mit einer Vielplatten-Vorrichtung verwendet werden kann, um eine hinreichende Zuführung des Strahlungssystems sicherzustellen.

[0068] Die Anwendung der Strahlung in der beschriebenen Art und Weise ermöglicht dem Patienten eine sofortige Befreiung (innerhalb von 6 Minuten) von jeglichen Schmerzen, welche unabhängig von den sie verursachenden Entzündungszuständen chemisch vermittelt werden, daß heißt, es gibt für andere Zustände, welche nicht durch Virus-Infektionen verursacht werden, eine Schmerzbefreiung. Sie beeinflusst nicht die Fortfüh-

rung der Schmerzimpulse, wie in der lokalen Anästhesie.

Experimentelle Ergebnisse

[0069] Beispiele der Erfindung werden nun in Bezug auf die Behandlung bestimmter Zustände beschrieben.

Herpes

[0070] Die strahlungsemitierende Oberfläche wurde für mindestens 90 Sekunden, typischerweise 4 Minuten, an den Fieberbläschen angeordnet. Die Umgebungszustände müssen derart sein, daß die Umgebungsstrahlung zu den Fieberbläschen unterhalb eines akzeptablen Niveaus verringert werden muß. Dies kann entweder durch Abschalten der Strahlung oder Ausbildung der Vorrichtung mit einem Flansch um das Äußere erreicht werden, wodurch das ultraviolette Licht auf den Bereich verringert wird. Die Behandlung findet nur einmal am Tag statt. Eine Behandlung könnte alles sein, was notwendig ist, da jedoch in Anbetracht der Tatsache, daß dies auch die Wundheilung verbessert und der Wundheilungs-Effekt, nur für 24 Stunden besteht, würden tägliche Behandlungen die klinische Wirkung verbessern. Unterschiedliche Wellenlängen wurden unter Verwendung einer Doppelblind-Vergleichsstudie untersucht, wobei den Kontrollpatienten Zovirax verabreicht wurde. Die durchschnittliche Behandlungszeit für einen Patienten, der mit 660 nm Strahlung behandelt wurde, betrug 7,5 Tage. Die durchschnittliche Behandlungszeit für einen Patienten, der mit 1072 nm Strahlung behandelt wurde, betrug 3 Tage, falls eine Läsion bereits vorhanden war. Jedoch betrug sie weniger als 12 Stunden, falls der Patient nur ein kribbelndes Gefühl aufwies.

[0071] 99,5% der Patienten beendeten ihren Anfall, falls sie innerhalb der Kribbel-Dauer unter Verwendung von 1072 nm Strahlung behandelt worden sind. Die Heilungsrate der Patienten, die eine Strahlungsbehandlung empfangen, war dahingehend vollständig, daß niemand ein Wiederauftreten seiner Fieberbläschen an der Behandlungsstelle aufwies. Jedoch 20% der mit Acyclovir behandelten Gruppe wiesen ein Wiederauftreten an der Behandlungsstelle auf.

[0072] Die Anzahl in der Studie betrug 300.

[0073] Eine weitere Studie wurde in einem Doppelblind-Protokoll durchgeführt, das die Strahlungsbehandlung mit Acyclovir vergleicht. Die Strahlungstherapie empfangende Gruppe hatte Fieberbläschen, die innerhalb von 4,7 Tagen ausheilten, und die Acyclovir empfangene Gruppe hatte Fieberbläschen, die innerhalb von 4,7 Tagen ausheilte. Die statistische Analyse ergab einen p-Wert von 0,027, welcher statistisch signifikant war.

[0074] Man beziehe sich bitte für weitere Details im folgenden auf die untere Tabelle.

Behandlung	Anzahl der Patienten	Durchschnittliche Heilungszeit (Tage)
Placebo-Bestrahlung plus Acyclovir	14	6,9
Aktive Bestrahlung	15	4,7
Aktive Strahlentherapie plus Placebo-Creme	16	6,7
Acyclovir	18	8,5
Rotlicht	20	7,5

Genitalherpes

[0075] Wiederum war der Applikator erforderlich, um den Konturen der Genitalien zu folgen, und bei einer Frau wurde die Zervix und die hintere Fornix gleichzeitig mit der Vagina und dem Perineum behandelt. Die Behandlungsdauer betrug nur 4 Minuten. Aufgrund der Form der Vorrichtung wird Umgebungsstrahlung von dem Behandlungsbereich ausgeschlossen, und ein verdunkeltes Zimmer ist nicht erforderlich.

[0076] Insgesamt wurden acht Patienten behandelt, wobei alle von einer geringeren Dauer des wiederauftretenden Genitalherpes-Angriffs berichteten. Zusätzlich waren alle Patienten nach einem Jahr Behandlungsdauer für jeden Angriff von einem Wiederauftreten für die letzten sechs Monate befreit, wohingegen sie typischerweise einen Angriff pro Monat hatten.

Gürtelrose

[0077] Die Strahlungsplatte wurde für Dauern von 4 Minuten an dem infizierten Bereich angebracht. Falls die Platte an der eigentlichen Hautoberfläche angebracht wird und die Platte optisch lichtundurchlässig ist, wird sie die Umgebungsstrahlung von dem Bereich ausschließen und daher einen erfolgreichen Ablauf der Behandlung ermöglichen. Die einzige Ausnahme, bei der ein verdunkeltes Zimmer erforderlich ist, ist für die Behandlung von Augenkrankheitszuständen, wenn jemand die Strahlungsemissionsoberfläche nahe dem Auge aufgrund der Wärmeerzeugung nicht haben kann. Die Wärmeerzeugung in Verbindung mit Augenkrankheitszuständen ist kontraindiziert. Ein Helm mit einem Detektor für Umgebungsstrahlung mit Alarm wurde verwendet, so daß die Strahlung dem kreisförmigen Bereich zugeführt werden kann. Die Behandlungs-Dauer betrug wieder 4 Minuten. Üblicherweise werden Augenkrankheitszustände auf einer täglichen Basis behandelt. Jedoch kann Augenerpes einmal alle drei Tage behandelt werden, um ein positives Ergebnis zu erzielen.

[0078] Vier Patienten wurden behandelt; alle hatten deutlich verkürzte Heilungsdauern und ein verringertes Eintreten oder Wiederauftreten.

Die gewöhnliche Erkältung

[0079] Der Patient wurde auf ein Bett gelegt, vorzugsweise in gedämpftem Licht, was jedoch nicht erforderlich ist. Die Vorrichtung wurde an der Haut angeordnet, wobei sichergestellt wurde, daß die Stirnhöhle, die Siebbeinzelle und die Kieferhöhle bedeckt sind. Eine andere Platte wurde am Hals angeordnet, um sicherzustellen, daß die Vorrichtung sich so hoch erstreckt wie der Winkel des Kiefers, um eine Behandlung des Rachenraumes und des Kehlkopfbereichs zu ermöglichen. Die Behandlungszeit betrug mindestens 4 Minuten. Nachdem dies abgeschlossen war, wurde eine orale Vorrichtung verwendet, die dem vaginalen Applikator ohne den Flansch sehr ähnlich ist. Die Vorrichtung wurde in den Mund des Patienten eingeführt. Die Behandlungsdauer betrug wieder 4 Minuten. Dieser Applikator weist eine austauschbare äußere Haut auf, die bei jedem Patienten gewechselt wird. Der Applikator wird den weichen Gaumen und den hinteren Bereich der oralen Rachenraumes behandeln und den oberen Bereich des Nasopharynx, wo der Oberflächen-Applikator kein akzeptables Tiefenwirkungsniveau erreichen würde. Unter Verwendung dieses Protokolls ist eine sofortige Linderung, d. h. innerhalb von 90 Sekunden, der Schmerzen in Verbindung mit einer Rachenentzündung erreicht worden, und die mit oraler Rachenentzündung verbundenen Symptome wurden innerhalb von sechs Stunden gelindert.

[0080] Zehn Patienten wurden behandelt. Zu bemerken ist, daß uneingeschränktes Licht dem Rachenraum mit unmittelbarer Linderung der Symptome zugeführt werden kann, jedoch für eine verbesserte Wirksamkeit ist es erforderlich, Licht der Wellenlänge 1072 nm zu dem Gesicht und den Höhlen zuzuführen. Wir bemerkten, daß sich in allen Fällen die Halsschmerzen sofort verbesserten und Symptome der Kongestion und einer grippeähnlichen Krankheit innerhalb von 4–6 Stunden gelindert wurden.

Akne

[0081] Unter Verwendung des gleichen Applikators kann heranreifende Akne durch einfaches Hinzufügen einer Kinnerweiterung behandelt werden. Die Behandlungszeit beträgt 4 Minuten. Umgebungslicht ist wichtig, jedoch nicht in dem Ausmaß, da der Applikator eine lichtundurchlässige Oberfläche aufweisen wird, so daß eine bloße Nähe zu der Haut das Umgebungslicht der Haut reduziert. Anwendungen sollten anfänglich alle zwei bis drei Tage stattfinden, und die Nachsorge wird vielleicht einmal in Woche betragen.

[0082] Zwölf Patienten wurden mit Licht des Lichttherapiesystems erfolgreich behandelt. Die Ergebnisse zeigen, daß, falls 950 nm/5 mm-Dioden verwendet wurden, eine merkliche Verschlimmerung des Krankheitsprozesses vorhanden war, jedoch bei Verwendung von 950 nm/8 mm-Dioden fand eine schwache Steigerung der Entzündung, jedoch insgesamt eine Verbesserung statt. Die Verwendung der eingeschränkten Strahlung führte zu einer schnellen Auflösung der Akne innerhalb von 7 Tagen. Eine tägliche Behandlung verbesserte die klinischen Ergebnisse. Sobald ein klinisches Ergebnis erzielt wurde, wurde die Kur für ein zufriedenstellendes Ergebnis für ein bis zwei Behandlungen pro Woche aufrechterhalten.

Muskelskelett-Beschwerden

[0083] Behandlung von Muskelskelett-Beschwerden, wie etwa des Tennisarms, Muskelverletzungen und Knieverletzungen. Die Behandlungszeit beträgt wieder nur 4 Minuten. Die Strahlung wird über den betroffenen Bereich gelenkt und ein sanfter Druck wird aufgebracht. Sobald die Behandlung abgeschlossen ist, fühlen sich die Patienten direkt schmerzfrei und weisen eine verbesserte Gelenkbeweglichkeit auf. Die Muskelsteifheit

wird außerordentlich verbessert. Dies ist ein deutlicher Vorteil bei der Behandlung von Gicht, da dies ein extrem schmerzhafter Zustand sein kann. Die Behandlung kann nach 24 Stunden wiederholt werden. Allgemein gesprochen ist eine Behandlung vor den 24 Stunden nicht angebracht, da kein zusätzlicher klinischer Vorteil vorhanden ist.

Postoperative Wunden

[0084] 24 Stunden nach einer Operation verringert eine 4-minütige Behandlungs-Dauer für 6–8 Stunden die Schmerzen, und dies wurde drei bis vier Mal am Tag wiederholt, um die Wundheilung zu verbessern. Die Behandlung kann auf täglicher Basis mit oder ohne den Schmerz hinsichtlich der postoperativen Wunde verwendet werden.

[0085] Sieben Freiwillige, die alle geringfügige Operationen hatten, stellten eine verringerte Narbenbildung fest, falls der Bereich des chirurgischen Einschnitts täglich für 10 Tage behandelt wurde, beginnend mit dem Tag der Operation. Daher ist es vorgesehen, daß die vorliegende Erfindung Anwendungen hat bei der Behandlung von Keloiden, Verbrennungen ("burns") und kosmetischen Operationen.

Bindegewebekrankheiten

[0086] Rheumatoide Arthritis ist ein Beispiel dieser Gruppe von Zuständen. Die schmerzhaften Bereiche werden in einer Vorrichtung behandelt, welche eine fixierte Platte, auf der die Hände angeordnet werden, und eine flexible Platte aufweist, die über den Händen angeordnet wird, wobei ein leichter Druck aufgebracht wird, um eine zusätzliche Durchdringung der Haut zu unterstützen. Die Behandlungszeit beträgt 4 Minuten. Die Umgebungsstrahlung tritt nicht als ein signifikanter Faktor bei der Behandlung von rheumatoider Arthritis auf. Teil des Behandlungsprotokolls kann auch die Behandlung von Thymus, Leber und regionalen Lymphknoten sein, die alle antigener Erkennung zugeordnet sind. Wiederum beträgt die Behandlungszeit 4 Minuten. Der Thymus, die Lymphknoten, die Leber und die Milz können einmal pro Woche behandelt werden, wohingegen die Hände anfänglich einmal pro Woche behandelt werden können. Jedoch können sie während einer akuten Verschlimmerung täglich behandelt werden. Falls sie mehr als einmal täglich behandelt werden, tritt kein Vorteil auf.

[0087] Eine kleine Studie, die acht Patienten in der rheumatologischen Klinik einbezieht, führte zu den Ergebnissen, daß diejenigen, die eine Placebo-Strahlungsbehandlung erhalten haben, sich deutlicher erleichtert fühlten als diejenigen, die eine aktive 950 nm-Strahlung erhalten haben. Jedoch bei Verwendung von Strahlung der eingeschränkten Wellenlänge gemäß der vorliegenden Erfindung berichteten alle zehn Patienten von einem klinischen Vorteil im Vergleich zu der Placebo-Behandlung. Zusätzlich haben wir entdeckt, daß, falls der Thymus und andere Aspekte des retikuloendothelialen Systems mit der eingeschränkten Strahlung behandelt wurden, die Patienten insgesamt eine Einstellung ihrer Arthralgie und der Myalgie erfuhren.

Bösartiger Tumor

[0088] Der Tumorbereich wird zusammen mit der Behandlung der Antigen-Erkennungszentren, wie Thymus, Milz, Leber und Lymphknoten behandelt. Tägliche Gesamtkörperbehandlungen können durchgeführt werden.

Bakterielle Infektionen

[0089] Eine Anzahl von diversen kleineren bakteriellen Infektionen wurden bei 35 Patienten erfolgreich behandelt. In allen Fällen war die Infektion für mindestens drei Tage vorhanden und wurde als sich täglich verschlimmernd erachtet. Während der Behandlungszeit hätte jeder Patient gewöhnlich ein orales Antibiotikum verschrieben bekommen. In 70% der Fälle ging die Infektion 6 Stunden nach der Behandlung zurück und war innerhalb eines Tages vollständig besser. In den verbleibenden 30% der Fälle hat sich die Infektion innerhalb eines Tages deutlich verbessert, und nach einer zweiten Strahlungsbehandlung war die Infektion am zweiten Tag verschwunden. Klinisch bemerkenswert war die Beobachtung, daß bei den behandelten Weißen ein deutlicher Abfall des oberflächlichen Narbengewebes an der angegriffenen Stelle vorhanden war. Wie zuvor bemerkt, war die uneingeschränkte 8 mm/950 nm-Dioden-Strahlungsquelle effektiv, jedoch nicht so effektiv wie die eingeschränkte Strahlung bei 1072 nm der vorliegenden Erfindung.

Sportmedizin

[0090] Die Behandlung von allen Muskelgruppen vor dem Training wird das Ausmaß bis zu 50%, steigern, bis zu dem der Athlet trainieren kann, zusätzlich zur Abnahme des Auftretens von Muskelverletzungen.

[0091] In einer Doppel-Blind-Studie wurden fünf Freiwillige verwendet, wobei eine Extremität mit Placebo-Strahlung und die entsprechende andere Extremität mit aktiver Strahlung behandelt wurden. In allen Fällen war es den Freiwilligen möglich, ihre Leistungstoleranz um 30–50% zu steigern, bevor sie sich muskelmüde in der mit aktiver Strahlung behandelten Extremität fühlten.

[0092] Muskelverletzungen wurden bei 35 Patienten erfolgreich behandelt. Die einbezogene Pathologie umfaßte das Rotatorenmanschetten-Syndrom, den Tennis-Arm, Schmerzen im unteren Rückenbereich und Lenden-Fasciitis. Die Wirksamkeit der Therapie erstreckte sich von einer sofortigen Befreiung in 30% der Fälle bis zu vollständiger Befreiung nach 24 Stunden bei den verbleibenden 70%. Eine tägliche Behandlung ist erforderlich, bis das Problem aufgelöst ist.

Augenkrankheitszustände

[0093] Chronische Augenschmerzen wurden bei 90% der elf behandelten Patienten erfolgreich dauerhaft gelindert.

[0094] Unstabiles Hornhaut-Epithel (über eine Dauer von 6 Wochen), das zu einer immer wiederkehrenden Hornhaut-Geschwürbildung führte, wurde bei 6 Patienten stabilisiert, wobei eine intakte Hornhaut-Oberfläche innerhalb von 5 Tagen nach Beginn der täglichen Strahlungstherapie-Behandlung gefördert wurde.

[0095] Vier Patienten mit Bindehautentzündung oder Trockenem-Augen-Syndrom berichteten von einer deutlich verringerten Augenirritation und erzeugten nach Strahlungsbehandlung deutlich geringere Ablagerungsanhäufungen innerhalb der Fornices. Zu bemerken war die Erfahrung, daß, während eine Strahlung bei 1072 nm bei diesem Zustand effektiv war, eine Strahlung bei 1268 nm effektiver war. Eine einmal wöchentliche Behandlung mit Strahlung war ausreichend, um die Symptome zu lindern.

[0096] Episkleritis und andere Entzündungszustände des Auges wurden bei 11 Patienten erfolgreich behandelt. Tägliche Behandlungen waren notwendig, um den erwünschten klinischen Effekt zu erzielen. Das Wiederauftreten der Entzündungszustände war in allen Fällen verringert. Alle behandelten Patienten litten über mehrere Monate an ihren Zuständen, und eine Auflösung trat ohne die Verwendung von Augentropfen innerhalb von 3–4 Tagen ein.

[0097] Schwere Ätzverletzungen am Auge werden als nicht behandelbar angesehen und führen nahezu immer zu der Zerstörung der Kornea und zur Blindheit. Tierexperimente (durchgeführt in Südafrika) haben gezeigt, daß Ätzverletzungen mit der Strahlung der vorliegenden Erfindung behandelbar sind.

[0098] Fünf Kaninchenaugenpaare wurden nach einer topischen Verabreichung eines Anästhetikums einer übersättigten NaOH-Lösung für 30 Sekunden ausgesetzt. Alle Augen wurden nach der Ätzverletzung gründlich ausgewaschen, und es wurde bemerkt, daß die Korneas sofort nach der Verletzung lichtundurchlässig waren. Ein Auge eines jeden Kaninchens wurde dann entweder mit gewöhnlichen Steroiden und Antibiotikum behandelt, während das andere Auge mit der Strahlung der vorliegenden Erfindung behandelt wurde. Alle Kaninchen wurden innerhalb von 4 Wochen nach einer zweifachen täglichen Behandlung geopfert. In allen Fällen entwickelten die Augen, die mit konventionellen Therapien (Steroide plus Antibiotikum) behandelt wurden, schnell eine Panophthalmie mit resultierender Blindheit, während die mit der Strahlungstherapie der Erfindung behandelten Augen zeigten, daß die vordere Kammer, Linse, der Glaskörper und die Retina intakt waren, trotz der Hornhaut-Zerstörung. Zusätzlich war das Narbengewebe im Vergleich zu den konventionell behandelten Augen in den strahlungsbehandelten Augen um mindestens 50% reduziert.

[0099] Weitere Experimente, die eine weniger konzentrierte NaOH-Lösung einbeziehen, die für eine längere Dauer von 3 Minuten aufgebracht wurde, führten zu einer Hornhaut-Zerstörung für alle Augen, wie an der blaß-milchigen Erscheinung der Korneas zu beurteilen war. Das gleiche Behandlungsprotokoll wurde angewendet, daß heißt, ein Auge wurde auf konventionelle Art und Weise behandelt und das andere durch Strahlungstherapie. Die Tiere wurden zwei Wochen nach der Behandlung geopfert und die Ergebnisse zeigten, daß die mit der Strahlungstherapie behandelten Augen klar waren, während die konventionell behandelten Augen lichtundurchlässig blieben.

[0100] Die Möglichkeit, die Narbenbildung zu verringern, wurde unter Verwendung von 5 Kaninchenaugenpaaren untersucht. Jedes Auge wurde mit einem geradlinigen 4 mm-Einschnitt voller Breite in das Zentrum der Hornhaut unter topischer Anästhesie vernarbt. Ein Auge wurde konventionell behandelt und das andere durch Strahlungstherapie. Alle Augen heilten, jedoch heilten die Strahlungstherapie empfangenen Augen mit einer

schnelleren Rate, wobei die Narbenbildung um 50% reduziert wurde. Es wurde bemerkt, daß eine Strahlung von 1072 nm die besten, ähnlichen Ergebnisse ergab.

Schmerz

[0101] Strahlung bei 950 nm war im Vergleich zu der eingeschränkten Strahlung bei 1072 nm und 1268 nm nur geringfügig effektiv. Es wurde bemerkt, daß bei der Behandlung von akutem Schmerz, der durch eine oberflächliche Verbrennung ("bum") verursacht wurde, eine 1072 nm-Strahlung effektiver war als eine 1268 nm-Strahlung. Jedoch wurde berichtet, daß 1268 nm-Strahlung effektiver war bei der Behandlung von tiefen Muskelschmerzen, verursacht durch Muskelverletzungen.

[0102] Der Schmerz der Patienten wurde durch subjektive Abschätzung beurteilt.

[0103] Daher ist es zu würdigen, daß das Strahlungstherapie-System der vorliegenden Erfindung einen weiten Anwendungsbereich bei der Behandlung einer Vielfalt unterschiedlicher Krankheiten und Zustände aufweist. Die Strahlungstherapie-System-Effekte auf einen Patienten werden schnell empfunden, und da das System nicht invasiv ist, bietet es dem Patienten eine weniger stressvolle/traumatische Therapie. Außerdem kann das System dazu verwendet werden, eine große Vielfalt von Patienten schnell zu behandeln, wodurch die finanziellen Belastungen des Gesundheitssystems reduziert werden.

Patentansprüche

1. System (4) zur Therapie mit elektromagnetischer Strahlung mit einem Mittel (2) zur Emission schmalbandiger divergenter elektromagnetischer Strahlung und welches geeignet ist, an der Behandlungsstelle eine Strahlungsintensität von mindestens 50 $\mu\text{Watt}/\text{cm}^2$ und bis zu 2 Watt/cm^2 zu erzeugen, **dadurch gekennzeichnet**, daß die Wellenlänge der elektromagnetischen Strahlung 1072 nm oder 1268 nm beträgt.

2. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 1, wobei der halbe Divergenzwinkel der elektromagnetischen Strahlung im Bereich von 15° bis 45° liegt.

3. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei die elektromagnetische Strahlung kontinuierlich oder gepulst ist.

4. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei im Falle einer kontinuierlichen elektromagnetischen Strahlung die Intensität für die Behandlung von Augen und Schleimhäuten mindestens 50 $\mu\text{Watt}/\text{cm}^2$ und bis zu 2 Watt/cm^2 beträgt.

5. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei im Falle einer kontinuierlichen elektromagnetischen Strahlung die Intensität für eine Hautbehandlung mindestens 500 $\mu\text{Watt}/\text{cm}^2$ und bis zu 2 Watt/cm^2 beträgt.

6. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–3, wobei für die Behandlung von Augen und Schleimhäuten im Falle einer gepulsten elektromagnetischen Strahlung die Spitzenintensität mindestens 50 $\mu\text{Watt}/\text{cm}^2$ und die mittlere Intensität bis zu 2 Watt/cm^2 beträgt.

7. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–3, wobei für eine Hautbehandlung im Falle einer gepulsten elektromagnetischen Strahlung die Spitzenintensität mindestens 500 $\mu\text{Watt}/\text{cm}^2$ und die mittlere Intensität bis zu 2 Watt/cm^2 beträgt.

8. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–3 oder 6 oder 7, wobei die mittlere Intensität der Intensität der gepulsten elektromagnetischen Strahlung im Bereich von 50–100 $\mu\text{Watt}/\text{cm}^2$ liegt.

9. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–4 oder 9–11, wobei die gepulste elektromagnetische Strahlung für Zeitdauern von mindestens 10–15 μ -Sekunden angewendet wird.

10. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–4 oder 6–9, wobei die gepulste elektromagnetische Strahlung bei einer Frequenz/Wiederholungsrate im Bereich von 480–800 Hz angewendet wird.

11. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 10, wobei die Frequenz/Wiederholungsrate 600 Hz oder ca. 600 Hz beträgt.
12. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 1–4 oder 6–11, wobei die gepulste elektromagnetische Strahlung auf den betroffenen Bereich für mindestens 30 Sekunden und bis zu 15 Minuten appliziert wird.
13. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei das System zur Therapie mit elektromagnetischer Strahlung auch ein Mittel aufweist, um den Betrag der Umgebungsstrahlung, welche auf die Behandlungsstelle auftrifft, zu verringern.
14. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 13, wobei das Mittel zum Ausschließen der Umgebungsstrahlung Strahlung unterhalb von 400–500 nm ausschließt.
15. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, ferner enthaltend ein Mittel, um die Intensität der Strahlung innerhalb eines vorbestimmten Bereichs zu halten.
16. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei die ausgegebene Strahlung mit einer sichtbaren Anzeige überwacht wird, welche die fehlerfreie Wirkungsweise der Vorrichtung sowohl hinsichtlich der Intensität als auch hinsichtlich der Wellenlänge anzeigt.
17. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, ferner enthaltend ein Mittel zur Steuerung/Regelung der Anwendungszeit der Strahlung.
18. System zur Therapie mit elektromagnetischer Strahlung nach einem der vorangehenden Ansprüche, wobei das Mittel zur Erzeugung der Strahlung Licht emittierende Festkörpervorrichtungen sind.
19. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 18, wobei die Licht emittierenden Festkörpervorrichtungen Licht emittierende Festkörperdioden oder Gasentladungs-Vorrichtungen oder eine Laserdioden-Vorrichtung sind.
20. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 18 oder 19, wobei die Strahlung von derartigen Vorrichtungen elektrisch betrieben oder über ein faser-optisches Zuführungssystem zu einem Applikator geführt wird.
21. System zur Therapie mit elektromagnetischer Strahlung nach einem der Ansprüche 18–20, wobei der Strahlungs-Emitter einen PN-Übergang enthält, der dazu ausgebildet ist, Strahlung mit einer Wellenlänge von 1072 nm oder 1268 nm zu emittieren.
22. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 21, wobei eine einzelne Leuchtdioden-Anordnung eine Vielzahl von ausgerichteten Übergängen enthält.
23. System zur Therapie mit elektromagnetischer Strahlung nach Anspruch 19, wobei die Gasentladungsvorrichtung eine Mischung von Gasen enthalten kann, die eine Ausgabe bei der gewünschten Wellenlänge von 1072 nm oder 1268 nm herbeiführt.

Es folgen 9 Blatt Zeichnungen

Anhängende Zeichnungen

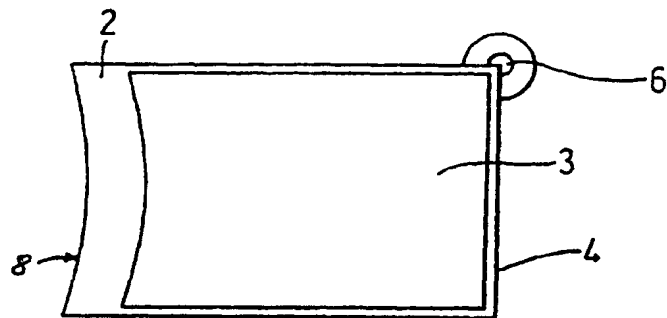


Fig. 1

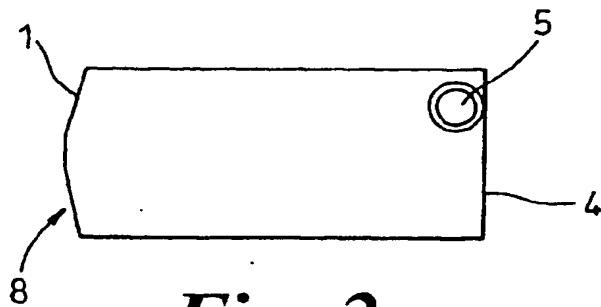


Fig. 2

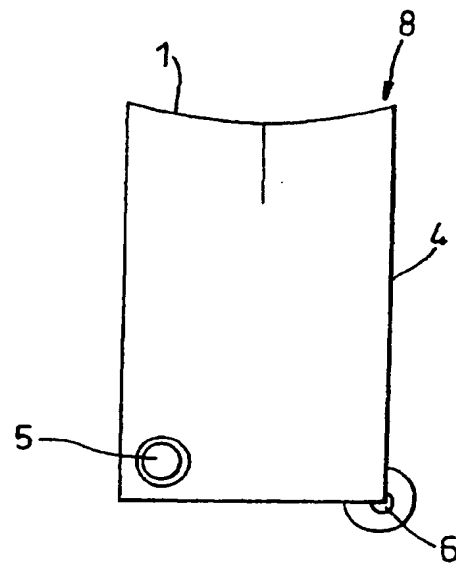


Fig. 3

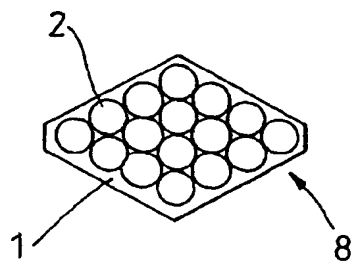


Fig. 4

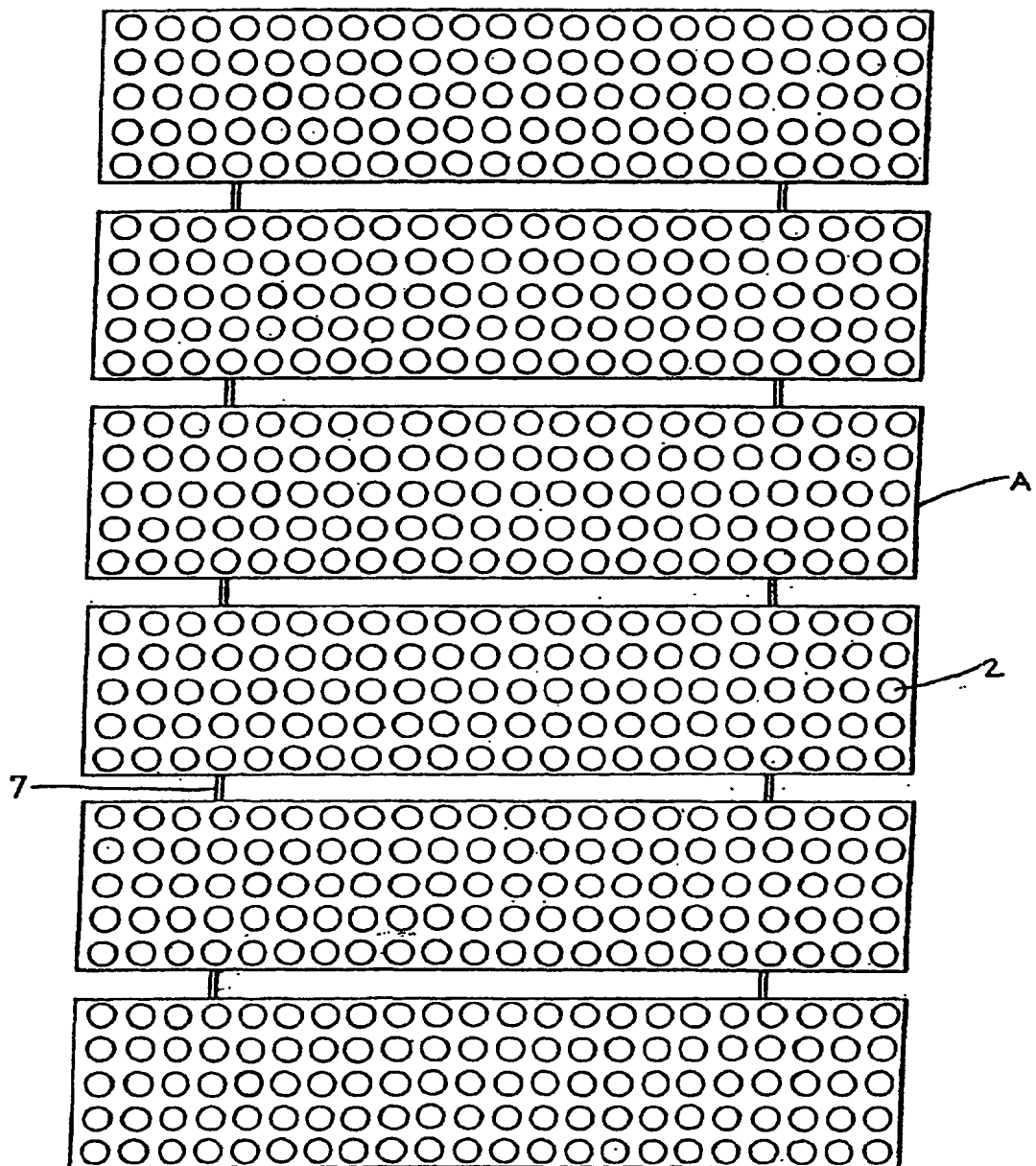


Fig. 5

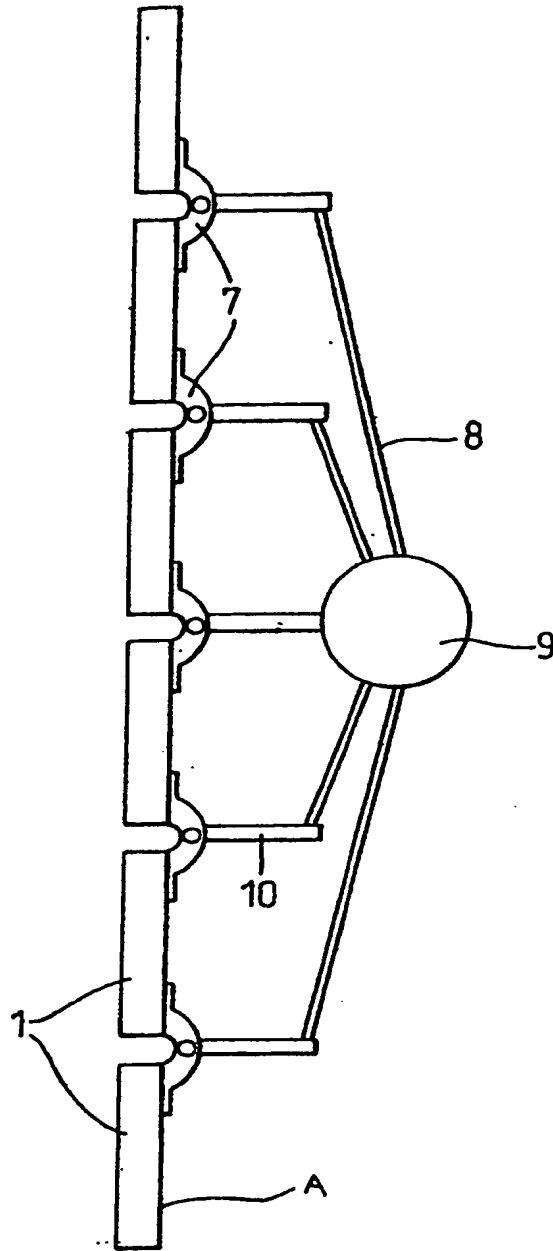


Fig. 6

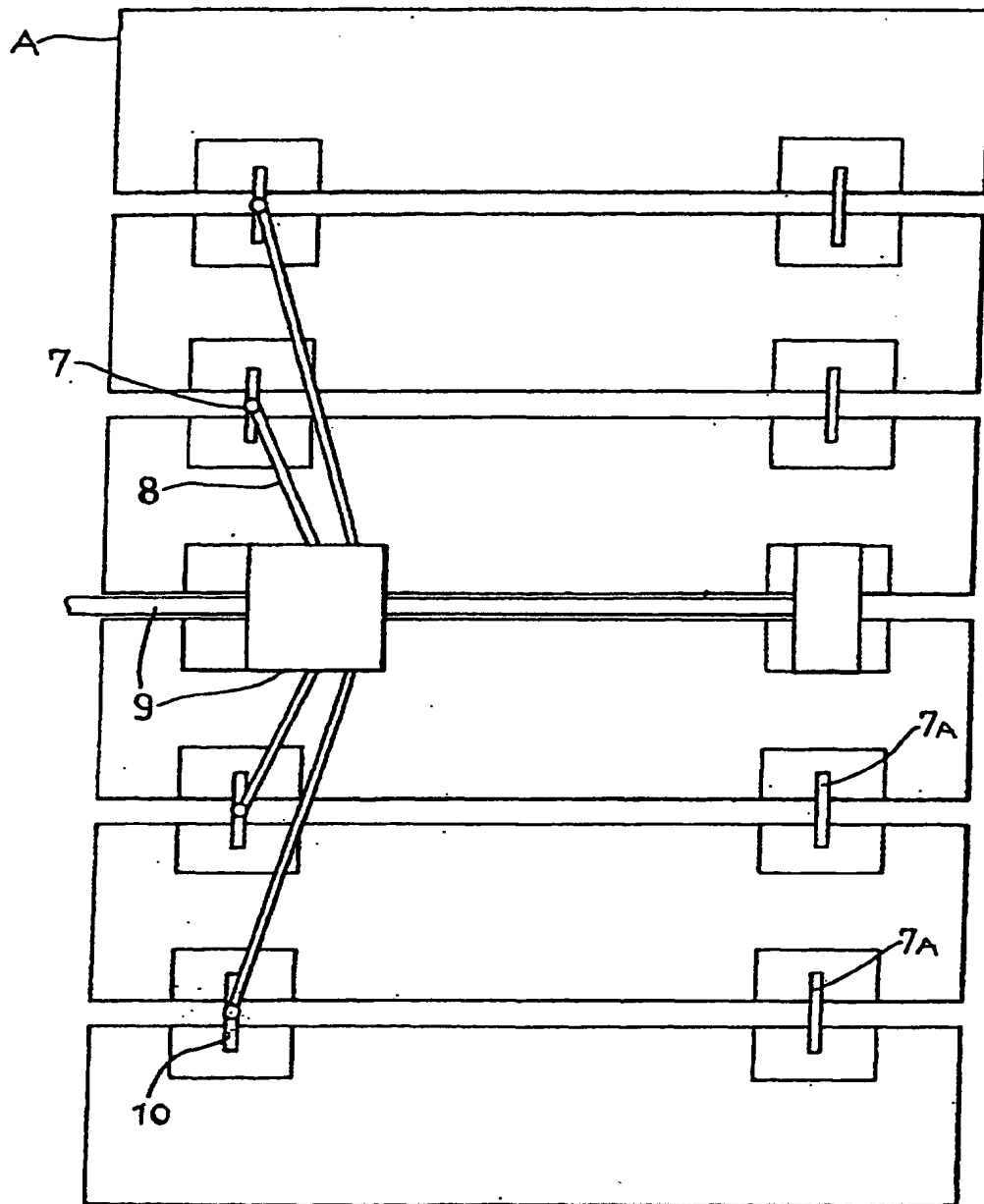


Fig. 7

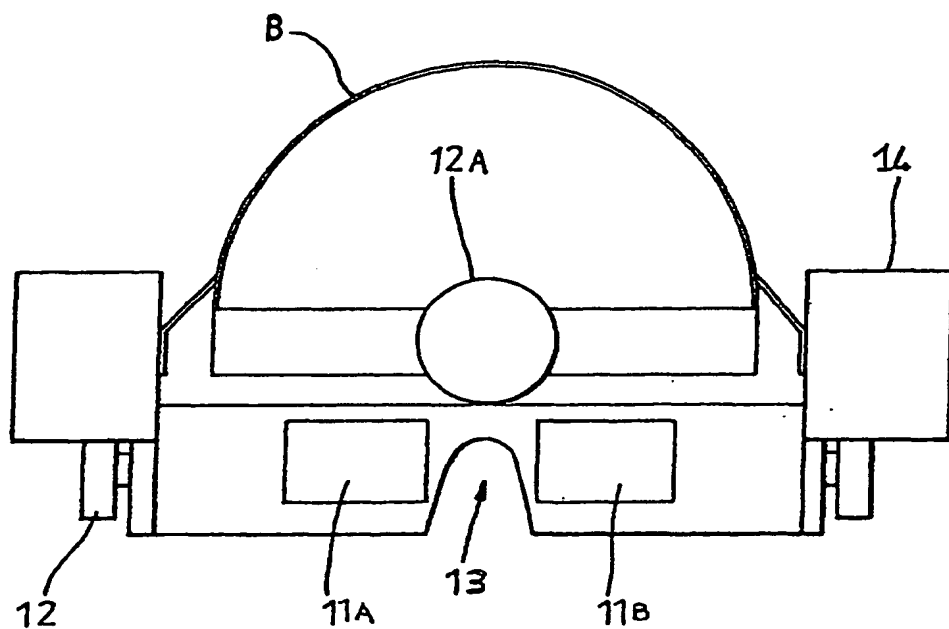


Fig. 8

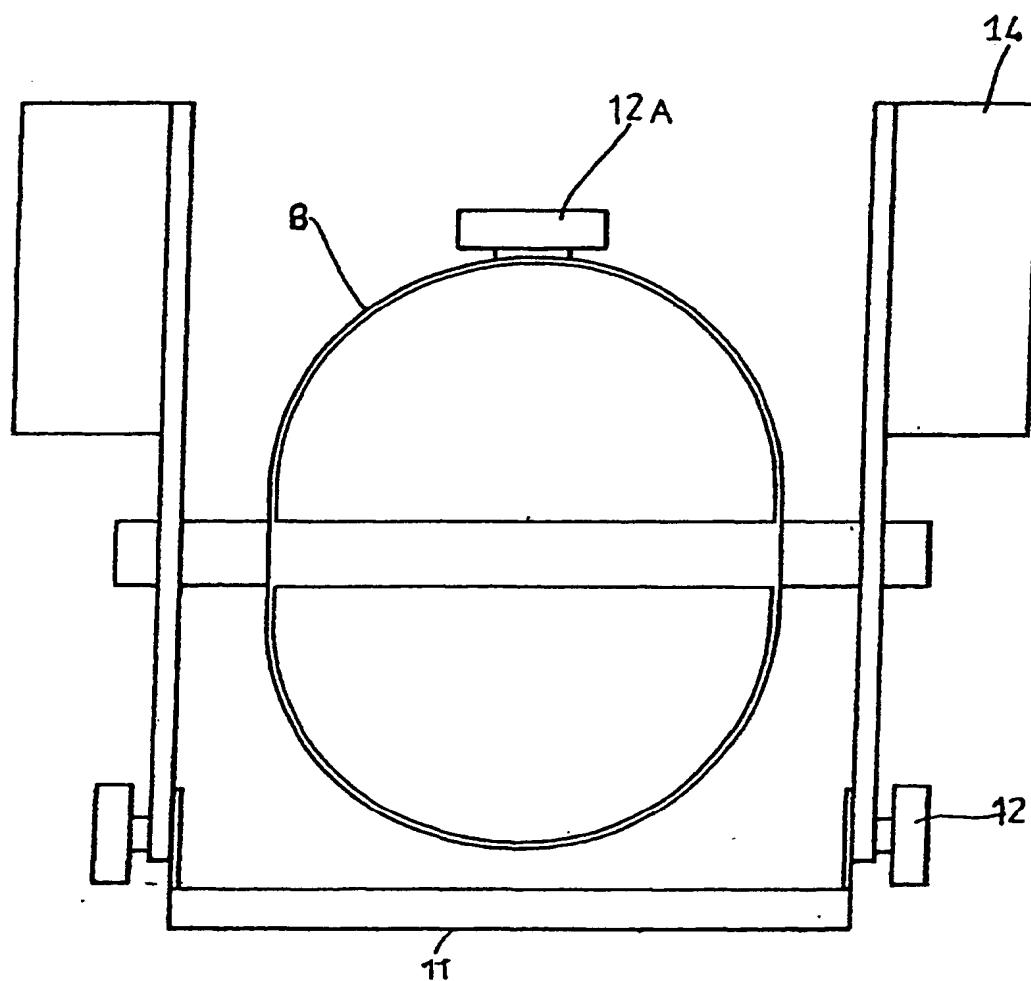


Fig. 9

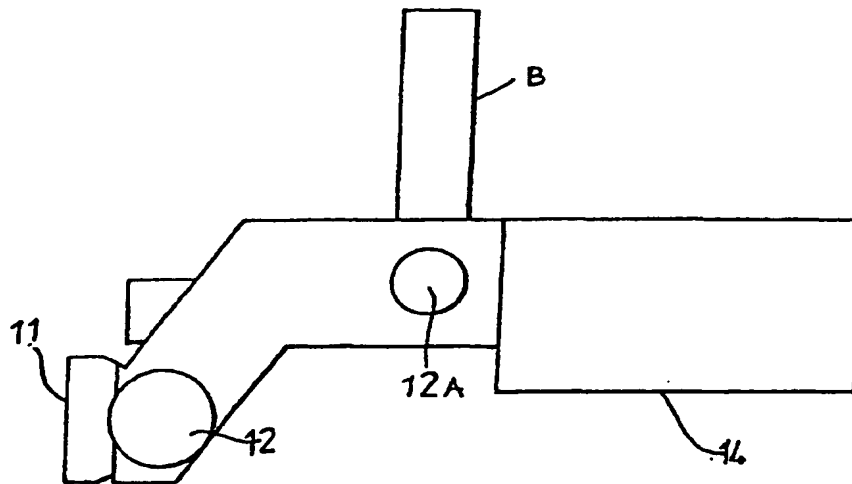


Fig. 10

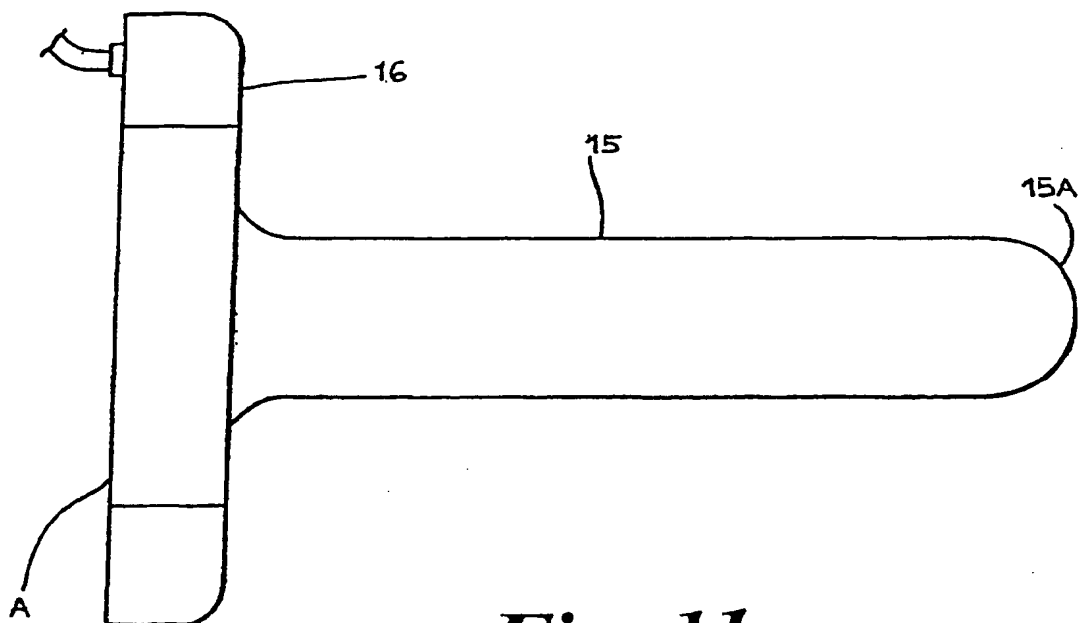


Fig. 11

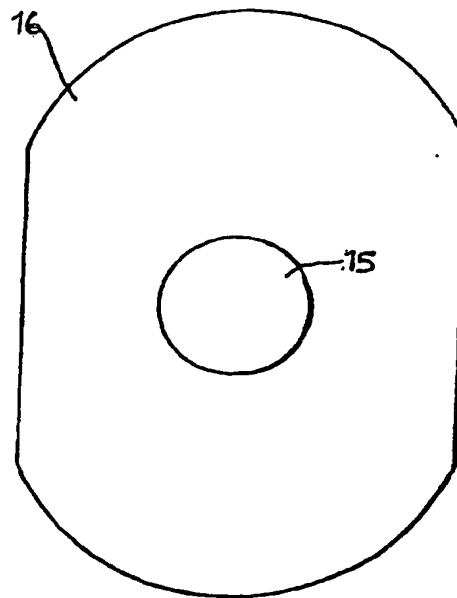


Fig. 12

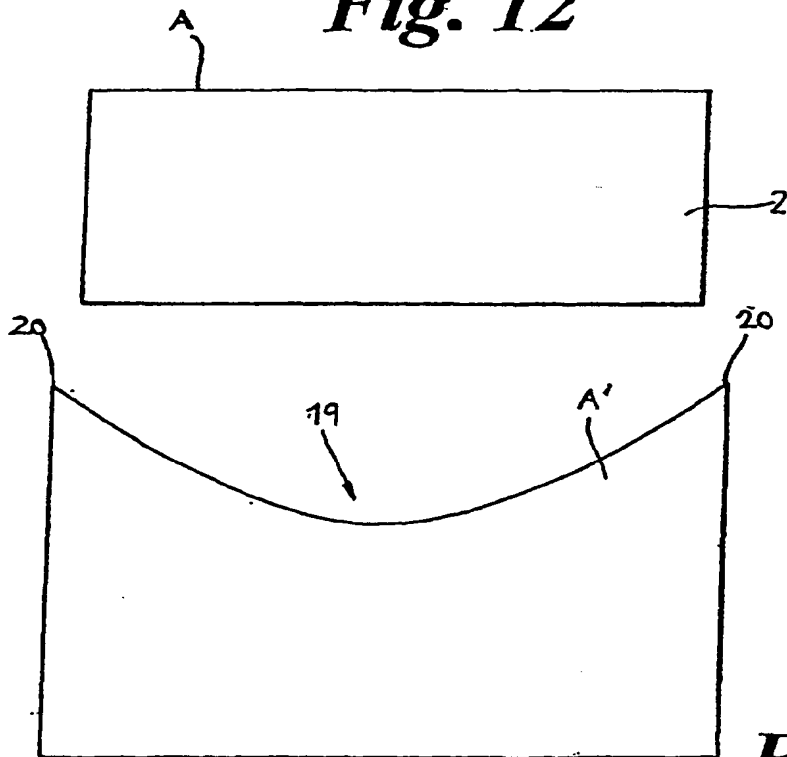


Fig. 13

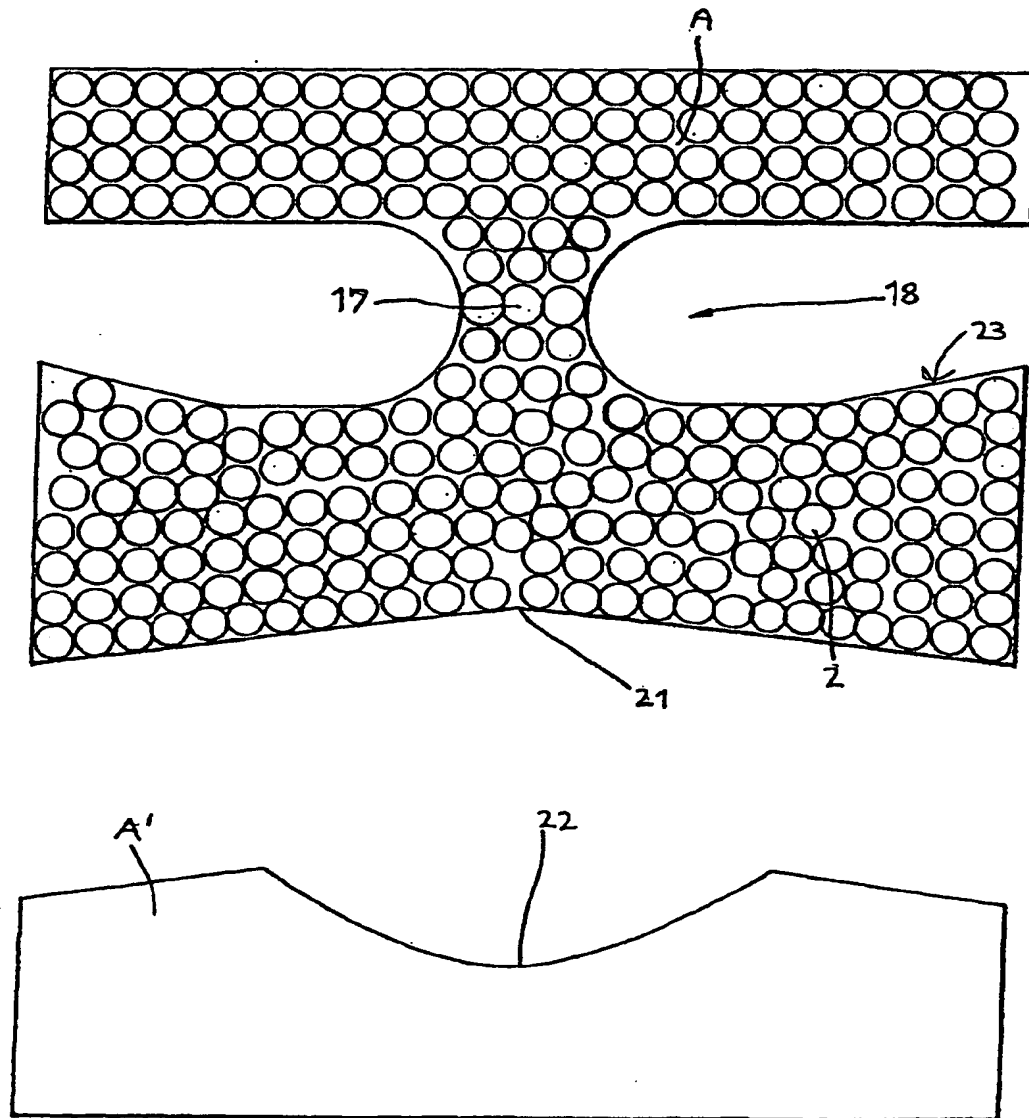


Fig. 14



Espacenet

Bibliographic data: WO9309847 (A1) — 1993-05-27

PHOTODYNAMIC STIMULATION DEVICE

Inventor(s): LARSEN ERIK [CH] $\pm$ (LARSEN, ERIK)

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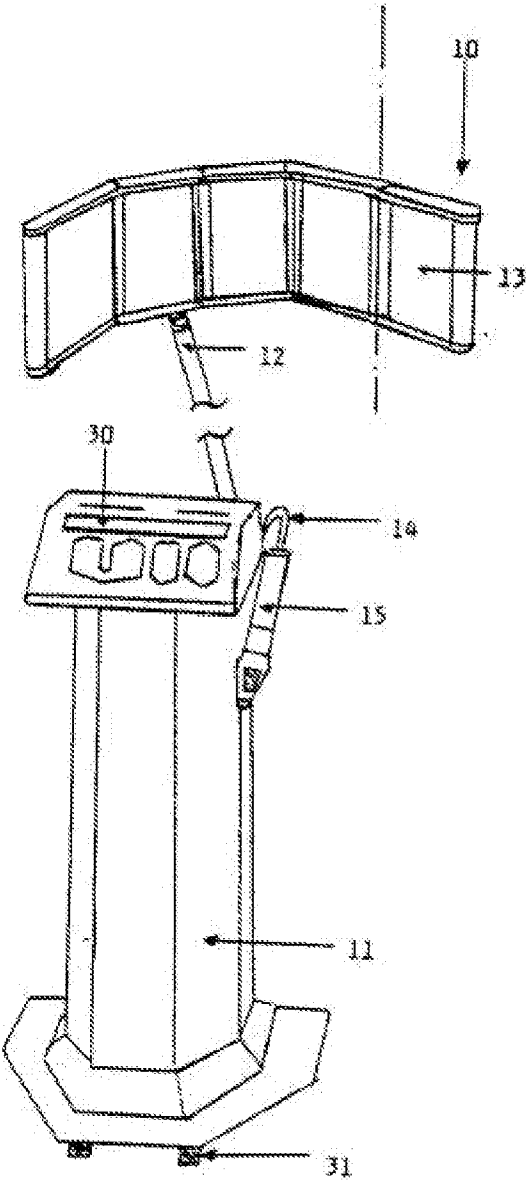
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Abstract of WO9309847 (A1)

Known devices which use infra-red radiation for the photodynamic stimulation of living cells, in particular human cells of both surface and underlying tissues, do not run at a constant energy output owing to the self-heating phenomena associated with infra-red semiconductor diodes. The device disclosed can run with constant output, thereby avoiding the drawbacks of known devices, by allowing shorter cut-in times for the diode pulses (17, 17a) and greater efficiency. An incidental effect of this is that a diode produces light in three wavelengths. Furthermore, blue light is produced in addition to infra-red and has a number of particularly useful therapeutic applications.





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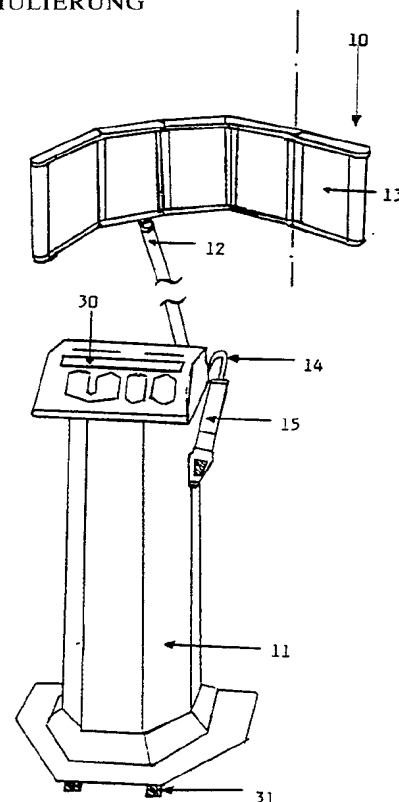
(54) Bezeichnung: VORRICHTUNG ZUR FOTODYNAMISCHEN ENERGIESTIMULIERUNG

(57) Abstract

Known devices which use infra-red radiation for the photodynamic stimulation of living cells, in particular human cells of both surface and underlying tissues, do not run at a constant energy output owing to the self-heating phenomena associated with infra-red semiconductor diodes. The device disclosed can run with constant output, thereby avoiding the drawbacks of known devices, by allowing shorter cut-in times for the diode pulses (17, 17a) and greater efficiency. An incidental effect of this is that a diode produces light in three wavelengths. Furthermore, blue light is produced in addition to infra-red and has a number of particularly useful therapeutic applications.

(57) Zusammenfassung

Bekannte Vorrichtungen zur fotodynamischen Stimulierung der Energie lebender, insbesondere menschlicher Zellen der oberflächlichen und tiefer liegenden Gewebeschichten mittels infraroter Strahlung sind auf Grund von Aufheizungerscheinungen von infraroten Halbleiterdioden nicht mit konstanter Energieabgabe betreibbar. Offenbart wird eine Vorrichtung, die mit konstanter Energieabgabe zur Meidung der Nachteile der bekannten Vorrichtungen betreibbar ist, indem kürzere Einschaltzeiten für Stromstöße zu den Dioden (17, 17a) und höhere Leistungen vorgesehen werden. Daneben ergibt sich daraus der Effekt, dass eine Diode Licht mit drei Wellenlängen abgibt. Ferner ist zu IR Licht auch Blaulicht für besondere vorteilhafte Anwendungen im Therapiebereich vorgesehen.



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Vorrichtung zur fotodynamischen Energiestimulierung

Die Erfindung betrifft eine Vorrichtung zur fotodynamischen Energiestimulierung nach dem Oberbegriff des Patentanspruches 1.

Mitochondrien in Zellen von Ein- und Mehrzellern stellen Orte energieliefernder Zellatmung dar. Auch sind sie in der Lage, Proteine zu synthetisieren, da sie über ein vom Zellkern ihrer Zelle unabhängiges, selbständiges genetisches System aus DNA und RNA verfügen. Hauptaufgabe der Mitochondrien ist jedoch die der Zellatmung, d.h. innerhalb der Zellen die Umsetzung von über die Blutbahn und sonstwie zugeführter Nährstoffe und Sauerstoff in Energie und körpereigene Baustoffe, wobei bei der Umsetzung auch Abfallprodukte, wie Wasser, Kohlendioxid, Alkohol und Milchsäure anfallen. Dabei spielt eine bedeutende Rolle die Adenosin-Triphosphorsäure (ATP), die von den Mitochondrien aus Adenosin Diphosphorsäure (ADP) und Orthophosphat synthetisiert wird. Komplizierte chemische Verbindungen spielen dabei als Reaktionskatalysoren eine entscheidende Rolle.

Anregung der Zellatmung, insbesondere Stimulierung der ATP Produktion von Zellen werden therapeutisch, vorzugsweise zur Förderung stark zellenenergieverbrauchender Heilungs- und Abmagerungsprozesse genutzt, hierunter fällt die Wundheilung, ferner auch die Reduktion der Schmerzempfindlichkeit, soweit durch eine krankheits- oder schwächebedingte Hypopolarisation bzw. Depolarisation ausgelöst. Ganz allgemein kann durch Anregung der Zellatmung durch Stress, Krankheit oder Alter ausgelösten Schwächen von Zellen entgegengewirkt werden. Damit mittels optischer Strahlung die Stimulierung der Mitochondrien möglich wird, sind zwei Voraussetzungen zu erfüllen.

Zum einen muß die Strahlung eine ganz bestimmte, die Stimulation auslösende Wellenlänge und Strahlungspulsfrequenz aufweisen, und zum anderen muß sie in der Lage sein, Gewebequerschnitte größerer Dicke zu durchdringen. Von der stimulierenden Strahlung ist ferner zu fordern, daß sie bestrahltes Gewebe nicht schädigt, auch soll sie keine Schmerzen erzeugen.

Bekannt ist eine Vorrichtung zur fotodynamischen Stimulierung der Energie von lebenden, vorzugsweise nicht pflanzlichen Zellen der oberflächlichen und insbesondere der tieferliegenden Gewebeschichten mittels infraroter Strahlung. Die Vorrichtung umfaßt ein Energieversorgungs- und Steuergerät und einen Applikator, an dem infrarote Strahlung im 900 nm (1 nm = 1 Nanometer) Bereich abstrahlende IR (Infrarot)-Halbleiterdioden und Reflektoren zur Bündelung der IR Strahlung vor dem Applikator vorgesehen sind. Das einen Generator umfassende Steuergerät speist bei dieser bekannten Vorrichtung die Halbleiterdioden mit Strompulsen einer bestimmten Frequenz, die innerhalb eines Bereiches von 500 - 5000 liegt.

Nachteilig bei der bekannten Vorrichtung ist, daß die Halbleiterdioden während des Betriebes einer Aufheizung unterliegen, die für die Vorrichtung einen Leistungsabfall nach sich zieht. Die bekannte Vorrichtung gibt mithin während des Betriebes keine konstante Leistung ab. Ein weiterer Nachteil liegt darin, daß infrarote Strahlung in nur einem Wellenlängen-Bereich von 900 nm verfügbar ist. Leistungsabfall und Strahlung in nur einem Wellenlängen-Bereich schränken die therapeutische Verwendbarkeit der bekannten Vorrichtung ein

Hiervon ausgehend, hat sich der Erfinder die Aufgabe gestellt, eine Vorrichtung zur fotodynamischen Energiestimulierung

lierung lebender Zellen zu schaffen, die im Betrieb eine konstante Leistung und zur Erweiterung ihrer therapeutischen Verwendbarkeit IR Strahlung in mindestens zwei Wellenlängen-Bereichen abgibt, und die Aufgabe wird gelöst durch eine gattungsgemäße Vorrichtung mit den kennzeichnenden Merkmalen des Anspruches 1

Vorteilhaft weitergebildet ist die Lösung durch die Gegenstände der dem Anspruch 1 folgenden Ansprüche.

Weitere Vorteile, Merkmale und Einzelheiten der Erfindung ergeben sich aus der folgenden Beschreibung eines bevorzugten Ausführungsbeispiels und der Zeichnungen, es stellen dar

Fig. 1: eine Darstellung der erfindungsgemäßen Vorrichtung in perspektivischer Darstellung.

Fig. 2 a,b,c: als Einzelheiten Maschinenapplikatoren der Vorrichtung gemäß Fig.1,

Fig. 3: einen Gelenkarm zur bewegbaren Anlenkung der Maschinenapplikatoren,

Fig. 4: ein Blockschaltbild einer Steuereinheit, die Applikatoren versorgt,

Fig. 5: ein Handapplikator,

Fig. 6: ein Applikator gemäß Fig. 5 mit axialer Lichtabstrahlung,

Fig. 7: ein Applikator gemäß Fig. 5 mit radialer Lichtabstrahlung,

Fig. 8: ein Applikator mit drehbarem Kopf,

Fig. 9: als Einzelheit einer Platine für den Applikator gemäß Fig. 8.

Gemäß Fig. 1 besteht die erfindungsgemäß ausgebildete Vorrichtung 10 zur fotodynamischen Stimulierung von Zellen aus einer Standsäule 11, an die über einen Gelenkarm 12 Maschinenapplikatoren 13 (folgend kurz Applikatoren 13 genannt) angelenkt sind. Die Standsäule 11 ist auch über eine elektrische Leitung 14 mit einem Handapplikator 15 verbunden. Die Standsäule 11, bevorzugt über Rollen 31 frei über eine Auflagefläche bewegbar, enthält das in Fig. 4 dargestellte Steuergerät 16, wobei Funktionen des Steuergerätes 16 auf einer Steuertafel 30 (auch Darstellgerät 30 genannt) einstell- und überwachbar sind.

Die Fig. 2a, 2b und 2c zeigen flächige Applikatoren 13, die als Ausführungsformen nach Fig. 2a bis 2c individuell einzeln, nebeneinander mehrfach oder in Kombination zu einem Applikator zusammengestellt sein können. Die Applikatoren 13 sind im Falle der Ausführungsform nach Fig. 2a mit Halbleiterdioden 17 und 17a (folgend kurz Dioden genannt) in versetzter Reihenfolge bestückt, wobei unter versetzter Reihenfolge eine Anordnung von Dioden 17 verstanden wird, derart, daß jeweils eine Diode 17a einer Reihe auf dem Schnittpunkt zweier Diagonalen durch jeweils zwei beidseitig benachbarter Dioden 17 angeordnet sind. Die Dioden 17 und 17a sind mit Reflektoren 18 umgeben, die Strahlungen sammeln und in einer wenige Zentimeter vor dem Applikator 13 liegenden Ebene bündeln.

Gemäß den Fig. 2b und 2c sind die Dioden 17 in regelmäßiger Reihenanordnung, d.h. zueinander aequidistant angeord-

net, wobei nach Fig. 2c ein Applikator 13 zusätzlich zu den Dioden 17 eine Lichtquelle 19 aufweist. Die Dioden 17 strahlen Licht mit drei Wellenlängen, nämlich 600, 900 und 1200 nm, also Infrarot (IR) Strahlung im Rotlichtbereich ab, während die Lichtquelle 19 in Form einer Röhre und die Dioden 17a (Fig. 2a) Licht mit einer Wellenlänge von 350-500 nm, d.h. Blaulicht abstrahlen.

Zur Behandlung großflächiger Gewebereiche sind gemäß Fig. 1 mehrere Applikatoren 13 über jeweils eine Längskante mit die Längskanten verbindenden Scharnieren 20 beweglich miteinander verbunden, wodurch die Applikatoren an Oberflächengestaltungen von Gewebereichen, z.B. an Rückenpartien von Menschen, für eine aequidistante Positionierung der Applikatoren 13 einstellbar werden. Der in Fig. 3 gezeigte Gelenkarm 12 verbindet einen oder mehrere Applikator(en) 13 mit der Standsäule 11. Der Gelenkarm 12 weist drei Gelenkträger 21, 22, 23 auf, wobei der Gelenkträger 21 einends mit der Standsäule 11, und der Gelenkträger 23 an einem freien Ende mit einem oder mehreren Applikatoren 13 bewegbar über ein arretierbares Gelenk 24 verbunden ist. Ein weiteres arretierbares Gelenk 25 verbindet Gelenkträger 23 mit 22, während der Gelenkträger 22 über ein Scharnier 26 mit dem Gelenkträger 21 verbunden ist. Letzterer Gelenkträger 21 ist seinerseits über ein Gelenk 27 mit der Standsäule 11 verbunden. Der Gelenkarm 12 gestattet somit die Positionierung der Applikatoren 13 vor oder über einem Gewebereich, ohne letzteren - durch Einhaltung eines Positionierungsabstandes - zu belasten. Der Gelenkarm 12 trägt weiter die elektrischen Zuleitungen 14 (nicht näher dargestellt) von dem in der Standsäule 11 aufgenommenen Steuergerät 16 zu dem oder den Applikator(en) 13.

Gemäß Fig. 4 besteht das Steuergerät 16 aus einem Generator 28, einem Zeiteinstellgerät 29 (Timer) und einem Dar-

stellgerät 30 (Display). Vermittels des Generators 28 werden die zur Erzeugung von Licht notwendigen Stromimpulse beigestellt, während über den Timer 29 alle Zeitfunktionen, beispielsweise auch die Behandlungsdauer einstellbar sind. Das Display 30 zeigt die gewünschten Behandlungsdaten, wie Strompulsfrequenz, Pulslänge und Pulshöhe an. Vermittels des Steuergerätes 16 ist die erfindungsmäßige Vorrichtung bezüglich Länge, Höhe und Frequenz von Stromstößen in relativ weiten Bereichen einstellbar, so daß als Lichtquellen Dioden 17, 17a und Röhren 19, wie auch Laserdioden gleicher Ausführung wie die beschriebenen Dioden 17 verwendbar werden. Zu diesem Zweck ist das Steuergerät für einen Betrieb mit Dioden 17 oder Laserdioden auf die eine oder andere Betriebsart, d.h. Halbleiterdioden - 17 oder Laserdiodenbetrieb umschaltbar ausgestaltet.

Für den Halbleiterdiodenbetrieb werden die Dioden 17 und gleichzeitig die Dioden 17a bzw. 19 für Blaulicht in entsprechender Anpassung mit Strom in Pulsfrequenzen von 200 bis 20'000 Hz mit Strompulslängen zwischen 2 und 200 Mikrosekunden, vorzugsweise zwischen 2 und 20 Mikrosekunden, und Strompulshöhen zwischen 12 und 25 Volt beaufschlagt. Bei dieser Betriebsweise, wegen der kurzen Strompulslängen, wird eine Aufheizung wirksam vermieden und dadurch ein leistungskonstanter Betrieb möglich. Gleichzeitig stellen sich bei vorstehender Betriebsart bei jeder Diode 17 gleichzeitig Lichtstrahlungen in drei einzelnen Wellenlängenbereichen, und zwar in Bereichen von 600, 900 und 1200 Nanometern ein. Durch gleichzeitige Anregung der Blaulicht-Dioden 17a, 19 stehen dann für therapeutische Zwecke vier Strahlungen mit Wellenlängen von 350-500 nm (Blaulicht) sowie 600, 900 und 1200 Nanometern zur Verfügung. Licht im Blaulichtbereich stimuliert Aktivitäten in Zellen und dadurch die Regeneration ermüdeten und kranken Gewebes, insbesondere den Abbau von Fettdepots bei Abmagerungstherapien. Die Hauptstrahlung kommt von den Infrarot Halblei-

terdioden 17. Strahlung im 600 Nanometerbereich stimuliert hauptsächlich die Zellatmung oberer Gewebeschichten, während die Strahlung im 900 Nanometerbereich Stimulationen von Zellen von der Geweboberfläche in bis zu ca. 70 mm tiefliegenden Gewebeschichten bewirkt. Die Strahlung im 1200 Nanometerbereich dringt noch tiefer als die 900 Nanometer-Strahlung in das Gewebe ein und stimuliert in einem lebenden Körper die Wasserabsorption.

Für die zweite Betriebsart - den Laserbetrieb - werden als Laserdioden ausgebildete Lichtquellen 17 mit Strompulsen einer Frequenz zwischen 200 und 20'000 Hz, einer Strompulslänge zwischen 2 und 200 Nanosekunden, vorzugsweise zwischen 2 und 20 Nanosekunden, und einer Strompulshöhe zwischen 40 und 400 Volt beaufschlagt. Erzeugt wird ein monochromatisches Laserlicht der Wellenlänge von ca. 900 Nanometern, das therapeutisch gleich wirksam wie das Licht vergleichbarer Wellenlänge von Halbleiterdioden 17 ist, sofern bei der Laserbetriebsart die Strompulslänge zur fotodynamischen Biostimulation in einem Längenbereich von 100 Nanosekunden gehalten ist. Bei Einstellung kurzer Pulslängen in dem Bereich von 2 bis 20 Nanosekunden und Einstellung einer hohen Betriebsspannung erfolgt von der Laserdiode 17 eine Doppelphotonabscheidung, die ihrerseits eine Blaulichtstrahlung in einem Wellenlängenbereich von ca. 350-500 Nanometern bewirkt. Mit Hilfe dieses Zweiphotonenwekzeuges in nahem Infrarotbereich kann die relativ große Energie des Blaulichtes, die normalerweise bereits auf der Hautoberfläche absorbiert wird, viel tiefer in das Gewebe transportiert werden. Während der Absorption von Doppelphotonen werden im Bereich des Blaulichtes Cytochrome aktiviert und Quantenenergien von 2.8 ev (Elektronenvolt) erreicht. Durch Doppelphotone wird auch die Aktivität der Chymotrypsin-Enzyme stimuliert.

Die Applikatoren 13 nach den Fig. 2a, 2b und 2c sind mit zwischen Dioden 17 - entweder Halbleiter- oder Laserdioden 17 - angeordneten Sensoren 32 versehen. Die Sensoren 32 dienen dem Zweck zu messen, welche Energiemenge ausgehend von den Applikatoren 13 in Joule/cm^2 in Gewebe eingedrungen ist. Für therapeutische Zwecke ist beispielsweise beabsichtigt, eine vorgegebene Energiemenge pro Flächeneinheit zu bestrahlendem Gewebe einzugeben, die zunächst am Steuergerät 16 eingestellt wird. Sensoren 32 messen nach Aufnahme der energiemäßig voreingestellten Strahlung durch das Gewebe die beispielsweise durch die Hautoberfläche teilweise abgestrahlte Energiemenge. Die voreingestellte abzüglich abgestrahlte Energiemenge ist diejenige Menge, die in Gewebe eindringt. Diese Energiemenge ist um den abgestrahlten Energiemengenanteil zu erhöhen, damit die therapeutisch vorgegebene Energiemenge zum Eintrag in das Gewebe gelangt.

Eine Erhöhung der einzutragenden Energiemenge ist mittels der erfindungsgemäßen Vorrichtung dadurch gegeben, daß entweder die Betriebsspannung (Pulshöhe) oder die Pulsfrequenz oder beide zusammen erhöht und/oder die Behandlungszeit durch Einstellung am Steuergerät 16 verlängert wird.

Während die Applikatoren 13 nach Fig. 2a, 2b und 2c zur Behandlung größerer Gewebeflächen gedacht sind, sind die Handapplikatoren 15a, 15b nach den Fig. 5 und 8 für kleinflächige Gewebebehandlungen vorgesehen.

Der Handapplikator 15a umfaßt einen zylindrischen Schaft 34, an dem ein Kopf 35 angeordnet ist. Im Kopf 35 ist eine Platine 36 mit Lichtquellen vorzugsweise Halbleiterdioden 17 (nicht dargestellt) vorgesehen. Auch angeordnet kann auf der Platine 36 sein eine Blaulicht-Halbleiterdiode 17a, die in gleiche Weise angeregt wird wie die Dioden der Applikatoren 13, so daß Licht 38 in Wellenlängen von 400, 600, 900 und 1200 Nanometern zur Verfügung steht, das gemäß

Fig. 7 aus einem Schlitz 37 aus dem Kopf austritt. Zur Polarisierung der Lichtstrahlen ist vor der Platine 36 ein Polarisierungsfilter 41 vorgesehen, dessen Verwendung den Vorteil bietet, daß die Strahlung besser in zu behandelndem Gewebe absorbiert wird. Der Kopf 35 weist auch eine vordere Strahlenaustrittsöffnung 39 auf. Im Kopf 35 vor der Austrittsöffnung 39 sind eine Linse zur Fokussierung der Lichtstrahlen 30 und ein Polarisierungsfilter 41 vorgesehen, wobei eine Lichtquelle (nicht gezeigt) gemäß Fig. 6 Licht 38 in axialer Richtung durch Linse 40 und Polarisierungsfilter 41 abstrahlt. Die Vorrichtung mit dieser Art Licht 38 - Abstrahlung eignet sich besonders zur Behandlung kleiner, punktförmiger Gewebeflächen.

Fig. 8 in Verbindung mit Fig. 9 stellen einen Handapplikator 15b dar, der sich besonders für Dentalbehandlungen eignet. Der Applikator 15b weist an dem vorderen Ende seines Schaftes 42 eine Platine 43 auf, die jeweils eine IR Licht-Halbleiterdiode 44 und Blaulicht-Halbleiterdiode 45 trägt, wobei die Diode 44 zur Abstrahlung von Licht mit den beschriebenen drei Wellenlängen und die Diode 45 zur Abstrahlung von Licht mit ebenfalls beschriebener Lichtwellenlänge angeregt wird. Vor der Platine 43 ist ein Kopf 46 mit einem am Kopf 46 angeordneten hohlen Ausleger angeordnet, in dem Glasfaser-Lichtkabel (nicht gezeigt) aufgenommen sind. Der Kopf 46 ist vor der Platine 43 drehbar ausgebildet, so daß der Ausleger 47 vor eine der beiden Dioden 44 oder 45 positionierbar ist. Wird der Ausleger 47 beispielsweise vor die Diode 44 positioniert, so durchläuft Licht der Wellenlängen 600, 900 und 1200 Nanometer das Lichtkabel, wird es am vorderen Ende des Auslegers 47 umgelenkt und trifft anschließend auf Gewebe, zum Beispiel Gewebe des Zahnfleisches auf, wodurch schmerzhaftes Zahnfleischveränderungen beseitigbar werden. Durch Positionierung des Auslegers 47 vor der

Blaulicht-Halbleiterdiode

45 wird Blaulicht durch den Ausleger 47 geleitet, mit dem aus Kunststoff bestehende Zahnfüllungen zur Härte bringbar sind. Es versteht sich, daß auch bei dieser Ausführungsform die Lichtstrahlungen durch Polarisationsfilter geleitet werden können. Auch ist es möglich, beide Handapplikatoren mit Sensoren zum gleichen Zweck wie im Zusammenhang mit den Applikatoren 13 beschriebenen auszustatten.

Patentansprüche

1. Vorrichtung zur fotodynamischen Stimulierung von Zellen, insbesondere Zellen menschlichen Gewebes, mittels Lichtstrahlung (38), bestehend aus einem Grundgerät (10) umfassend ein Steuergerät (16) mit einem Generator (28) und mindestens einem Lichtquellen aufweisenden Applikator (13, 15a, 15b) mit Reflektoren (18) zur Bündelung der Lichtstrahlen (38) vor dem Applikator (13, 15a, 15b), wobei das Steuergerät (16) mit Generator (28) zur Speizung der Lichtquellen mit Strom in Pulsen einer Frequenz zwischen 200 und 20.000 Hz, einer zeitlichen Strompulslänge zwischen 2 Nanosekunden und 20 Mikrosekunden und einer Strompulshöhe zwischen 12 und 400 Volt ausgebildet sind.
2. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß die Lichtquellen infrarote Strahlung abgebende Halbleiterdioden (17) sind.
3. Vorrichtung nach Anspruch 2, dadurch gekennzeichnet, daß jede Halbleiterdiode (17) infrarote Strahlung in mindestens zwei Wellenlängenbereichen abgibt.
4. Vorrichtung nach Anspruch 3, dadurch gekennzeichnet, daß jede Halbleiterdiode (17) infrarote Strahlung in Wellenbereichen von etwa 600, 900 und 1200 Nanometern abgibt.
5. Vorrichtung nach einem der Ansprüche 1 bis 4, dadurch gekennzeichnet, daß der Applikator mindestens eine Lichtquelle (17a, 19) aufweist, die Licht mit einer Strahlung in einem Wellenlängenbereich von etwa 350-500 Nanometern abgibt

6. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß die Lichtquellen als Infrarotlicht mit einer Wellenlänge von ca. 900 nm emitierende Laserdioden (17) ausgebildet sind.
7. Vorrichtung nach einem der Ansprüche 1 bis 6, dadurch gekennzeichnet, daß die Applikatoren als flächige Maschinenapplikatoren (13) oder Handapplikatoren (15) ausgebildet sind.
8. Vorrichtung nach Anspruch 7, dadurch gekennzeichnet, daß die Maschinenapplikatoren (13) aus mehreren Einzelapplikatoren bestehen, die über Scharniere (20) zueinander in Winkeln verstellbar sind.
9. Vorrichtung nach einem der Ansprüche 1 bis 8, dadurch gekennzeichnet, daß Applikatoren (13) an einer Standsäule (11) über einen Gelenkarm (12) beweglich angeordnet sind.
10. Vorrichtung nach einem der Ansprüche 1 bis 9, dadurch gekennzeichnet, daß Applikatoren (13, 15a, 15b) Sensoren (32) aufweisen.
11. Vorrichtung nach einem der Ansprüche 1 bis 10, dadurch gekennzeichnet, daß die Applikatoren (15a, 15b) als Handapplikatoren ausgebildet sind.
12. Vorrichtung nach Anspruch 11, dadurch gekennzeichnet, daß ein Handapplikator (15a) einen Schaft (34) mit einem am Schaft angeordneten Kopf (35) umfaßt, im Kopf (35) eine Platine (36) mit Halbleiter- und/oder Laserdioden und ein PolarisierungsfILTER (38) zwischen der Platine (36) und einem Schlitz (37) zum Austritt

der Lichtstrahlung (38) aus dem Kopf (35) vorgesehen sind.

13. Vorrichtung nach dem Anspruch 12, dadurch gekennzeichnet, dass der Kopf (35) einends eine in axialer Erstreckung des Kopfes (35) abstrahlende Lichtquelle mit einer Linse (40) und einem Polarisierungsfiler (41) zwischen Lichtquelle und Strahlenaustrittsöffnung (39) aufweist.
14. Vorrichtung nach Anspruch 11, dadurch gekennzeichnet, daß der Handapplikator (15b) zwischen einem Kopf (46) und Schaft (42) eine mit mindestens einer IR (44) und einer Blaulicht (45) emitierender Diode ausgestattete Platine (43) aufweist, der Kopf (46) vor der Platine (43) drehbar ausgebildet und entweder das Infrarot- oder Blaulicht über einen Ausleger (47) zu einem Behandlungsort leitbar ist.
15. Vorrichtung nach Anspruch 14, dadurch gekennzeichnet, daß der Ausleger (47) ein lichtleitendes Glasfaserkabel enthält.

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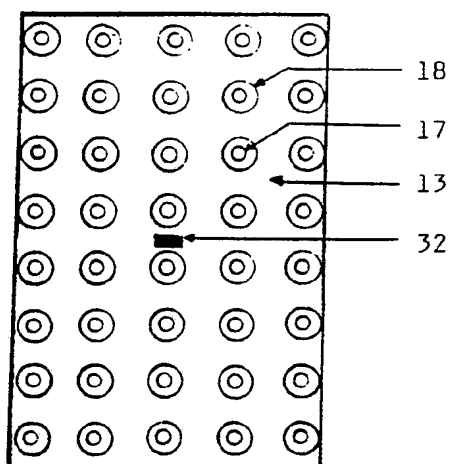


Fig. 2b

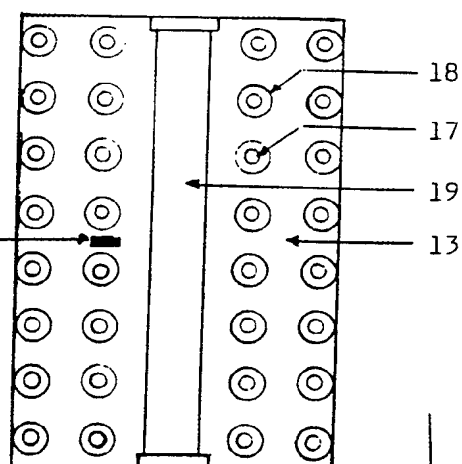


Fig. 2c

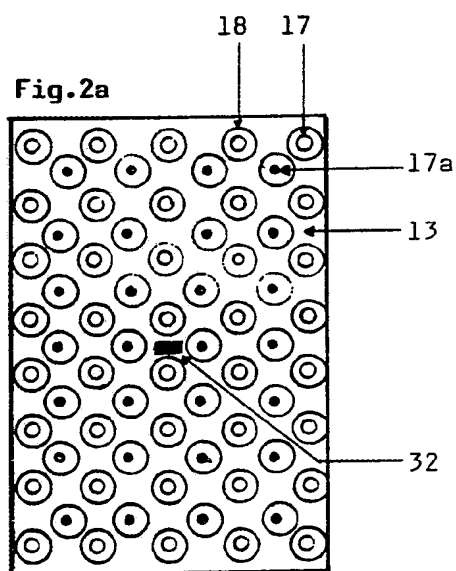


Fig. 2a

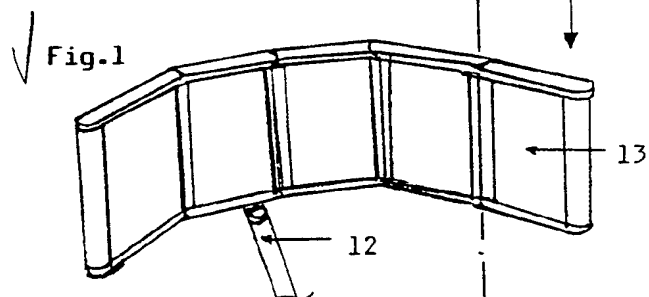


Fig. 1

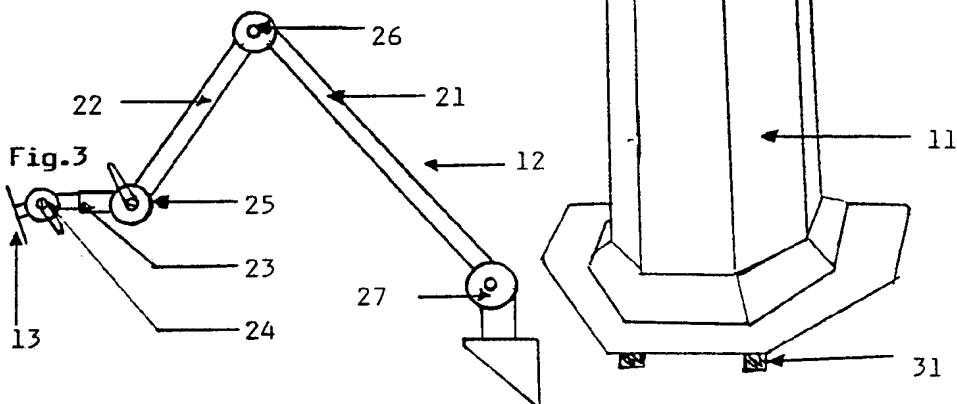
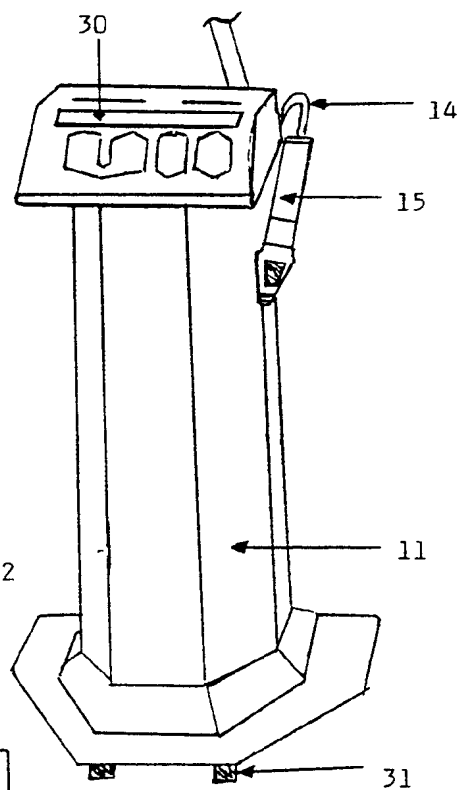
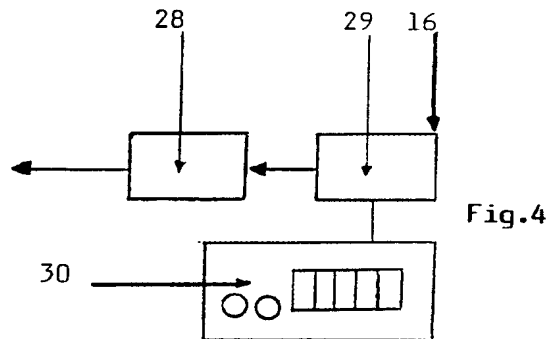
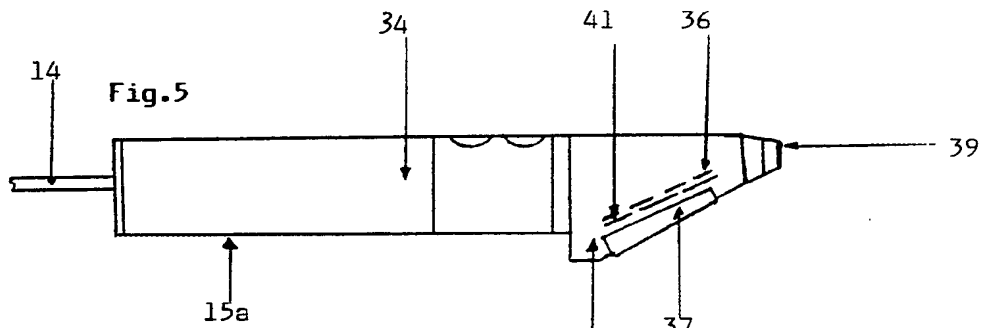
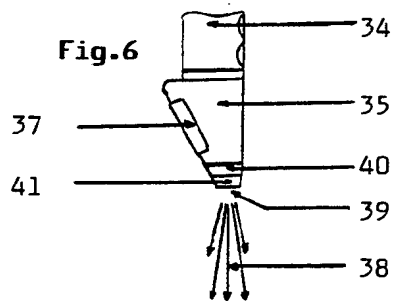
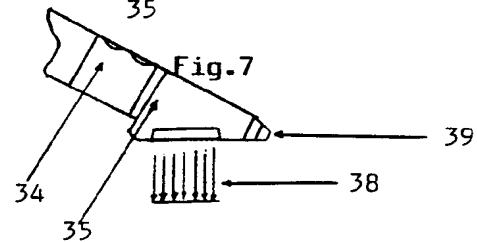
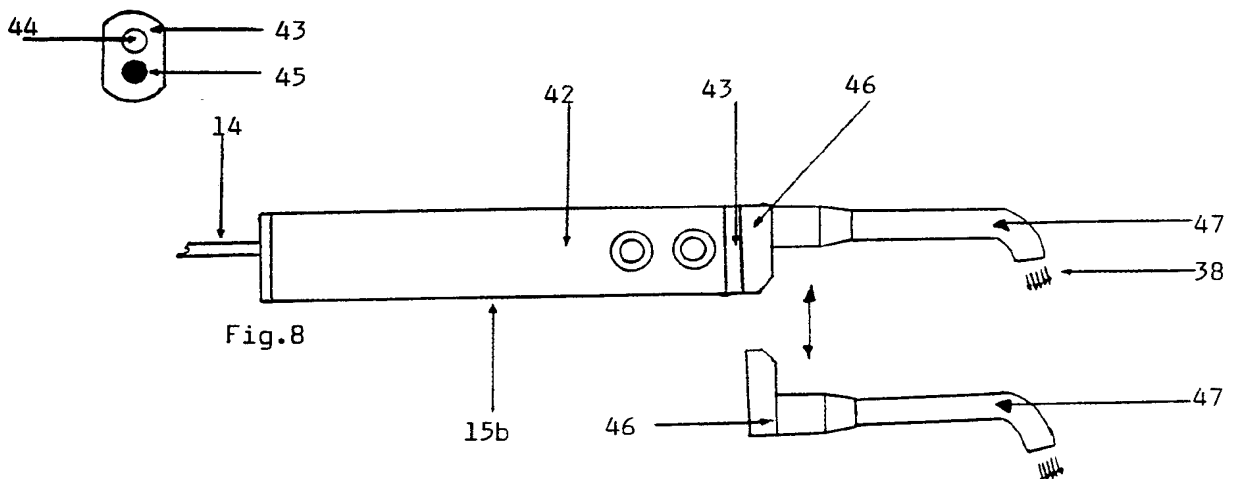


Fig. 3



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ERSATZBLATT

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CH 92/00228

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl.⁵ A 61 N 5/06

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)

Int.Cl.⁵ A 61 N

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	DE, U, 8 813 852 (NORMEDICA) 29 December 1968 see page 3, line 1 - page 7, line 30; figures 1-3	1,2,6-9
A	---	4
A	DE, A, 4 012 854 (HECHT, SCHUHMANN) 25 October 1990 see column 2, line 53 - column 3, line 1; figures 1,2	1,2
A	---	1-4,6,7,11,12
A	EP, A, 0 320 080 (DIAMANTOPOULOS, ALEXANDROU) 14 June 1989 see page 3, line 55 - page 8, line 37; figures 4-8	11,12,15
A	---	
A	DE, U, 8 628 810 (HEITLAND INTERNATIONAL COSMETICS) 15 January 1987 see page 8, line 2 - line 12; figure 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 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

11 March 1993 (11.03.93)

Date of mailing of the international search report

14 April 1993 (14.04.93)

Name and mailing address of the ISA

European Patent Office

Authorized officer:

Facsimile No.

Telephone No.

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

CH 9200228
SA 67730

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 11/03/93

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE-U-8813852	29-12-88	None	
DE-A-4012854	25-10-90	None	
EP-A-0320080	14-06-89	US-A- 4930504 JP-A- 1136668	05-06-90 29-05-89
DE-U-8628810	15-01-87	None	

EPO FORM P0479

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

I. KLASSIFIKATION DES ANMELDUNGSGEGENSTANDS (bei mehreren Klassifikationssymbolen sind alle anzugeben) ⁶		
Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC Int.Kl. 5 A61N5/06		
II. RECHERCHIERTE SACHGEBIETE		
Recherchierter Mindestprüfstoff ⁷		
Klassifikationssystem	Klassifikationssymbole	
Int.Kl. 5	A61N	
Recherchierte nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Sachgebiete fallen ⁸		
III. EINSCHLAGIGE VERÖFFENTLICHUNGEN ⁹		
Art. ^o	Kennzeichnung der Veröffentlichung ¹¹ , soweit erforderlich unter Angabe der maßgeblichen Teile ¹²	Betr. Anspruch Nr. ¹³
X	DE,U,8 813 852 (NORMEDICA) 29. Dezember 1988 siehe Seite 3, Zeile 1 - Seite 7, Zeile 30; Abbildungen 1-3	1,2,6-9
A	---	4
A	DE,A,4 012 854 (HECHT,SCHUHMANN) 25. Oktober 1990 siehe Spalte 2, Zeile 53 - Spalte 3, Zeile 1; Abbildungen 1,2	1,2
A	EP,A,0 320 080 (DIAMANTOPOULOS,ALEXANDROU) 14. Juni 1989 siehe Seite 3, Zeile 55 - Seite 8, Zeile 37; Abbildungen 4-8	1-4,6,7, 11,12

	-/--	
^o Besondere Kategorien von angegebenen Veröffentlichungen ¹⁰ : "A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist "E" Älteres Dokument, das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist "L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt) "O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht "P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist "T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist "X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden "Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren anderen Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist "&" Veröffentlichung, die Mitglied derselben Patentfamilie ist		
IV. BESCHEINIGUNG		
Datum des Abschlusses der internationalen Recherche	Absenddatum des internationalen Recherchenberichts	
11.MAERZ 1993	14. 04. 93	
Internationale Recherchenbehörde	Unterschrift des bevollmächtigten Bediensteten	
EUROPAISCHES PATENTAMT	HERBELET J.C.	

III. EINSCHLAGIGE VERÖFFENTLICHUNGEN (Fortsetzung von Blatt 2)		
Art °	Kennzeichnung der Veröffentlichung, soweit erforderlich unter Angabe der maßgeblichen Teile	Betr. Anspruch Nr.
A	DE,U,8 628 810 (HEITLAND INTERNATIONAL COSMETICS) 15. Januar 1987 siehe Seite 8, Zeile 2 - Zeile 12; Abbildung 1 -----	11, 12, 15

**ANHANG ZUM INTERNATIONALEN RECHERCHENBERICHT
ÜBER DIE INTERNATIONALE PATENTANMELDUNG NR.**

CH 9200228
SA 67730

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentedokumente angegeben.

Die Angaben über die Familienmitglieder entsprechen dem Stand der Datei des Europäischen Patentamts am
Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

11/03/93

Im Recherchenbericht angeführtes Patentedokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE-U-8813852	29-12-88	Keine	
DE-A-4012854	25-10-90	Keine	
EP-A-0320080	14-06-89	US-A- 4930504 JP-A- 1136668	05-06-90 29-05-89
DE-U-8628810	15-01-87	Keine	

EPO FORM P473

Für nähere Einzelheiten zu diesem Anhang : siehe Amtshlatt des Europäischen Patentamts, Nr.12/82

Electronic Acknowledgement Receipt

EFS ID:	43027196
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	18-JUN-2021
Filing Date:	14-FEB-2020
Time Stamp:	12:30:28
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	119786	no	3
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Warnings:

Information:					
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Information:					
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3	Foreign Reference	DE69827286.pdf	2493751	no	23
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Warnings:					
Information:					
4	Foreign Reference	WO93_09847.pdf	2395437	no	24
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5	Non Patent Literature	BRAATHEN.pdf	17669262	no	19
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6	Non Patent Literature	DRAGIEVA.pdf	5161617	no	5
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Warnings:					
Information:					
7	Non Patent Literature	KURWA.pdf	3423946	no	5
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8	Non Patent Literature	MACCORMACK.pdf	10409937	no	11
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BIOFRONTERA EXHIBIT 1035

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10	Non Patent Literature	WOLF.pdf	2965604	no	5
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11	Non Patent Literature	EPSrchRpt_060221.pdf	585752	no	8
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Warnings:					
Information:					
12	Non Patent Literature	NoA_0405.pdf	1363636	no	10
			fa3c0304c4103fa3eede3a0deaaf6fde10acc5cc		
Warnings:					
Information:					
Total Files Size (in bytes):			72097004		
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: CENTRAL, DOCKET
Art Unit: 3600
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents G6 and G7 listed on the attached PTO/SB/08 were cited as being relevant during the prosecution of a European application. A copy of the Extended European Search Report dated June 2, 2021 is submitted herewith (document G14).

Document G15 listed on the attached Form PTO/SB/08 is a PTO Notice of Allowance issued in a co-pending case (serial no. 16/438,702). A copy of the Office Action is being submitted herewith.

English abstracts are provided for documents G6 and G7. Documents G8-G13 are in English.

Documents G1 and G7; and G2 and G6 belong to the same “patent families,” respectively, whereby the English language documents may assist the PTO in understanding the content of the non-English language document.

Unless otherwise indicated, no English translation is readily available (not considering machine-generated translations that may be freely available online, to both the Applicant and the PTO) for each of the non-English language documents. However, a commercially available English language abstract is provided herewith, where indicated on the attached Form PTO/SB/08. Inasmuch as Applicants have endeavored to provide at least one item that complies with the requirement for a “concise explanation of relevance” for each of the non-English language documents, each of these documents has been submitted in compliance with the PTO requirements and should be considered by the Examiner (37 CFR §1.97, §1.98 and MPEP §609).

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date June 18, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: July 9, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

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 ⁶
	H1	Britannica, The Editors of Encyclopaedia, "Gel: Physics and Chemistry", 4 pages, July 20, 1998, and "Gel: Additional Information", 1 page, Available on line at: https://www.britannica.com/science/gel and https://www.britannica.com/science/gel/additional-info#history	
	H2	FEHR ET AL., Photodynamic Therapy of Vulvar and Vaginal Condyloma and Intraepithelial Neoplasia Using Topically Applied 5-Aminolevulinic Acid, Lasers in Surgery and Medicine, 2002, 30:273-279, 7 pages	
	H3	FEHR ET AL., Selective Photosensitizer Distribution in Vulvar Condyloma Acuminatum After Topical Application of 5-Aminolevulinic Acid, Am. J. Obstet. Gynecol., Volume 174(3), March 1996, pages 951-957	
	H4	HURLIMANN ET AL., Photodynamic Therapy of Superficial Basal Cell Carcinomas Using Topical 5-Aminolevulinic Acid in a Nanocolloid Lotion, Pharmacology and Treatment, Dermatology 197, 1998, pages 248-254	
	H5	REINHOLD ET AL., A Randomized, Double-Blind, Phase III, Multicentre Study to Evaluate the Safety and Efficacy of BF-200 ALA (Ameluz®) vs. Placebo in the Field-Directed Treatment of Mild-to-Moderate Actinic Keratosis with Photodynamic Therapy (PDT) When Using the BF-RhodoLED® Lamp, British Journal of Dermatology, 175(4): 696-705, February 27, 2016, 10 pages	
	H6	Third Party Submission filed in Application No. 17/109,311, June 21, 2021, 21 pages	

Examiner Signature		Date Considered	
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Electronic Acknowledgement Receipt

EFS ID:	43210741
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	09-JUL-2021
Filing Date:	14-FEB-2020
Time Stamp:	14:20:22
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	116834	no	2
			04581fdb8b8ed812109eaf49d2f4b94a6589e352		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	109909	no	1
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	BRITANNICA.pdf	395632	no	5
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Warnings:					
Information:					
4	Non Patent Literature	FEHR.pdf	1548430	no	7
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Information:					
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Information:					
6	Non Patent Literature	HURLIMANN.pdf	1579959	no	7
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Warnings:					
Information:					
7	Non Patent Literature	REINHOLD.pdf	1667419	no	10
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Warnings:					
Information:					
8	Non Patent Literature	ThirdParty_Submission.pdf	1358508	no	21
			763fed2658b10649a3137ffd200d917e468834e8		
Warnings:					
Information:					

BIOFRONTERA EXHIBIT 1035

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: CENTRAL, DOCKET
Art Unit: OPAP
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents H1-H6 listed on the attached PTO/SB/08 comprise a Third Party Submission in Application Serial No. 17/109,311, filed June 21, 2021.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 9, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 19, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	OPAP
				Examiner Name	CENTRAL, DOCKET
Sheet	1	of	1	Attorney Docket Number	067286-0410

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)			
	I1	2016/0346392-A1	12-01-2016	WULF, HANS CHRISTIAN	
	I2	2020/0100997-A1	04-02-2020	SOLER ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

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 ⁶
	I3	USPTO Notice of Allowance, 17/009,871 (067286-0411), 7/22/2021, 14 pages	
	I4	USPTO Notice of Allowance, 17/109,311 (067286-0419), 08/10/2021, 14 pages	
	I5	USPTO Office Action, 17/109,311 (067286-0419), 07/20/2021, 17 pages	

Examiner Signature		Date Considered	
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Electronic Acknowledgement Receipt

EFS ID:	43553738
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	19-AUG-2021
Filing Date:	14-FEB-2020
Time Stamp:	15:33:06
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	IDSTrans.pdf	117172	no	2
			e6ed9e61501f91e80ca452c99dd3287863af735c		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	106612 9fe5c160a4eae82d1cedb462a87caec5b08d02a	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	NoA_0411.pdf	1646903 a8cfbe6010d76568588bcbe20b3e6fe7720fbb19	no	14
Warnings:					
Information:					
4	Non Patent Literature	NoA_0419.pdf	1238721 85eb49b93ee21ea60d4e9f525e47e33d6940029b	no	14
Warnings:					
Information:					
5	Non Patent Literature	FOA_0419.pdf	1694717 0f1ad3546e00a755700051082f66a88a4781e933	no	17
Warnings:					
Information:					
Total Files Size (in bytes):			4804125		
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: CENTRAL, DOCKET
Art Unit: OPAP
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), before the mailing date of the first Office Action on the merits.

CONCISE EXPLANATION OF RELEVANCE

Documents I1 and I2 listed on the attached Form PTO/SB/08 were cited in a PTO Notice of Allowance of a co-pending case (serial no. 17/109,311). The relevance of the references can be found in the PTO Notice of Allowance of the co-pending case. A copy of the Notice of Allowance is being submitted herewith (document I4).

Document I3 listed on the attached Form PTO/SB/08 is a PTO Notice of Allowance issued in a co-pending case (serial no. 17/009,871). A copy of the Notice of Allowance is being submitted herewith.

Document I5 listed on the attached Form PTO/SB/08 is a PTO Office Action issued in a co-pending case (serial no. 17/109,311). A copy of the Office Action is being submitted herewith.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date August 19, 2021

By /Glenn Law/

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Glenn Law
Attorney for Applicant
Registration No. 34,371



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	10/25/2021		
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			10/25/2021	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):

ipdocketing@foley.com

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.

Information Disclosure Statement

2. Applicant should note that the large number of references in the attached IDS have been considered by the examiner in the same manner as other documents in Office search files are considered by the examiner while conducting a search of the prior art in a proper field of search. **See MPEP 609.05(b).** Applicant is requested to point out any particular references in the IDS which they believe may be of particular relevance to the instant claimed invention in response to this office action.

Drawings

3. The Applicant is reminded to carefully review the drawing figures and the accompanying specification to ensure that all reference numerals present in the drawing figures are defined within the specification.

Specification

4. The disclosure is objected to because of the following informalities: the first paragraph of the specification should be updated to indicate the present status of all applications referred to therein.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. 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.

6. Claims 1-20 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 applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

7. Claim 1 recites the limitation "nested hinges configured to reduce optical dead space" in lines 2-3. The metes and bounds of the claim are unclear as it is not known what the optical dead space is compared to in order to know that it has been "reduced".

8. Claim 6 recites the limitation "nested hinges configured to reduce optical dead space" in line 3. The metes and bounds of the claim are unclear as it is not known what the optical dead space is compared to in order to know that it has been "reduced".

9. Claim 8 recites the limitation "output of the illumination over an active emitting area is within 60% of maximum over all operation distances" in lines 1-2. The metes and bounds of the claim are unclear, as it is unknown what is meant by "output of the illumination", what the maximum is of, and to what "operation distances" refers.

10. Claim 9 recites the limitation "output of the illumination over an active emitting area is within 70% of maximum over a distance of two and four inches" in lines 1-2. The metes and bounds of the claim are unclear, as it is unknown what is meant by "output of the illumination", what the maximum is of, and to what "a distance of two and four inches" refers. Is the distance intended to be between two and four inches or intended to be a distance of two inches and a distance of four inches?

11. Claim 10 recites the limitation "output of the illumination over an active emitting area is within 80% of maximum over a distance of two and four inches" in lines 1-2. The metes and bounds of the claim are unclear, as it is unknown what is meant by "output of the illumination", what the maximum is of, and to what "a distance of two and four inches" refers. Is the distance intended to be between two and four inches or intended to be a distance of two inches and a distance of four inches?

12. Claim 18 recites the limitation "light sources of the illuminator" in lines 1-2. It is unclear if this is referring to the light sources recited in claim 6 or different light sources.

13. Claim 19 recites the limitation "a nested hinge" in line 2. It is unclear if this is one of the nested hinges recited in claim 6 or a different nested hinge.

Claim Rejections - 35 USC § 102

14. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention.

16. Claims 1, 2, 6, 7, 13, 18, and 19 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by Tobin (U.S. 2007/0283655, cited by Applicant). Regarding claim 1, Tobin discloses a system for photodynamically diagnosing or treating a patient, comprising: an illuminator 100 comprising at least five panels 101/102/103/107/108 connected by nested hinges 104/105 configured to reduce optical dead space (see Figures 2, 2A, 3B, 4, 5B, 6B, and 9, where the hinges are considered "nested" because they are formed of components fitted one inside the other, and the reduction of optical dead space is relative to if a larger gap was present between panels), light sources 910-912 disposed on a surface of the illuminator (see Figure 9), the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources (see paragraph [0040], line 9), one of the at least five panels positioned as a center panel 101 configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel (see Figures 3B, 4, 5B, 6B, 7B, 8B, and 9).

17. Regarding claim 2, Tobin discloses that the illuminator is configured to uniformly illuminate the treatment surface when the treatment surface is at a distance of two to four inches from the illuminator (see paragraph [0040], line 9).

18. Regarding claim 6, Tobin discloses a method of photodynamically diagnosing or treating a patient, comprising: positioning an illuminator 10 proximate to the patient (see Figures 3B, 4, 5A/B, 6A/B, 7B, 8B, and 9) the illuminator comprising at least five panels 101/102/103/107/108 connected by nested hinges 104/105 configured to reduce optical dead space (see Figures 2, 2A, 3B, 4, 5B, 6B, and 9, where the hinges are considered “nested” because they are formed of components fitted one inside the other, and the reduction of optical dead space is relative to if a larger gap was present between panels); and uniformly illuminating a treatment surface of the patient with the illuminator (see Figures 3B, 4, 5A/B, 6A/B, 7B, 8B, and 9, and paragraphs [0003], [0004], and [0040]).

19. Regarding claim 7, Tobin discloses that the nested hinges are mounted to inner side surfaces of adjacent panels (see Figure 2).

20. Regarding claim 13, Tobin discloses that at least one panel includes tabs, spacers 106, outwardly extending from a top side and a bottom side (spaces 106 are on both sides of center panel 101, which can be called the top side and the bottom side), the tabs being configured to receive an adjacent panel therein (spacers 106 are connected to side panels via hinges 104 and are thus considered to be “configured to receive an adjacent panel therein”).

21. Regarding claim 18, Tobin discloses changing intensities of light sources of the illuminator with a controller in accordance with information received from at least one sensor relating to a curvature of the treatment surface (see paragraph [0039], lines 18-25).

22. Regarding claim 19, Tobin discloses that at least one panel includes a recess configured to receive a flange of a nested hinge (the recess is considered the hole in the panel that accepts adjustment screws 204 and 205, which are considered the “flange” of the nested hinge).

23. Claims 1, 2, 5-7, and 18 are rejected under 35 U.S.C. 102(a)(1) as being anticipated by Larsen (U.S. 2005/0075703, cited by Applicant). Regarding claim 1, Larsen discloses a system for photodynamically diagnosing or treating a patient, comprising: an illuminator comprising at least five panels 13 connected by nested hinges (called 10 in the disclosure of Larsen and indicated as 20 in Figure 1 of Larsen, see paragraphs [0027], lines 5-8 and [0072], lines 1-3) configured to reduce optical dead space (see Figure 1, where the hinges are considered “nested” because they are not visible between the panels and the panels are flush against each other where the hinges are indicated, and the reduction of optical dead space is relative to if a larger gap was present between panels), light sources 17/18 disposed on a surface of the illuminator (see Figures 2A-D), the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources (see paragraph [0072], which describes that operation of the device as “without leaving any unradiated gaps”), one of the at least five panels positioned as a center panel configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel (see Figure 1).

24. Regarding claim 2, Larsen discloses that the illuminator is adjusted such that there are no unradiated gaps (see paragraph [0072]) and, thus, it is respectfully submitted that the illuminator is configured to uniformly illuminate the treatment surface when the treatment surface is at a distance of two to four inches from the illuminator.

25. Regarding claim 5, Larsen discloses that a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm (see paragraph [0071]).

26. Regarding claim 6, Larsen discloses a method of photodynamically diagnosing or treating a patient, comprising: positioning an illuminator 10 proximate to the patient (see Figure 1), at least five panels 13 connected by nested hinges (called 10 in the disclosure of Larsen and indicated as 20 in Figure 1 of Larsen, see paragraphs [0027], lines 5-8 and [0072], lines 1-3) configured to reduce optical dead space (see Figure 1, where the hinges are considered “nested” because they are not visible between the panels and the panels are flush against each other where the hinges

are indicated, and the reduction of optical dead space is relative to if a larger gap was present between panels); and uniformly illuminating a treatment surface of the patient with the illuminator see paragraph [0072], which describes that operation of the device as “without leaving any unirradiated gaps”).

27. Regarding claim 7, Larsen discloses that the nested hinges are mounted to inner side surfaces of adjacent panels (see paragraph [0072], lines 1-4).

28. Regarding claim 18, Tobin discloses changing intensities of light sources of the illuminator with a controller in accordance with information received from at least one sensor 32 relating to a curvature of the treatment surface (see paragraphs [0030] and [0079]).

Claim Rejections - 35 USC § 103

29. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

30. 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, 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.

31. The factual inquiries 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.

32. 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.

33. Claims 3-5 are rejected under 35 U.S.C. 103 as being unpatentable over Tobin (U.S. 2007/0283655, cited above) in view of Harth et al. (U.S. 2003/0216795). Tobin discloses the invention substantially as claimed, but fails to disclose that that the illuminator is configured to output red light at an intensity of about 30 J/cm² to about 150 J/cm², the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm², or a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm. Harth teaches a method and apparatus for providing photodynamic therapy to a patient to treat acne (see Abstract) that includes applying light using an illuminator configured to output red light at an intensity of 20 J/cm², which is considered to be “about” 30 J/cm² (paragraph [0185], lines 5-6) and output light at an irradiance density of 10 mW/cm² to 30 mW/cm² (see paragraph [0123], lines 10-12), and a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm (see Abstract and paragraph [0020], lines 5-6). It would have been obvious to one having ordinary skill before effective filing date of the claimed invention to modify the invention of Tobin such that the illuminator is configured to output red light at an intensity of about 30 J/cm² to about 150 J/cm², the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm², and a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm, as taught by Harth, as it has been held

that combining prior art elements according to known methods to yield predictable results requires only routine skill in the art. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742, 82 USPQ2d 1385, 1396 (2007).

34. Claims 11, 12, and 14-17 are rejected under 35 U.S.C. 103 as being unpatentable over Tobin (U.S. 2007/0283655, cited above) in view of Tapper et al. (U.S. 2013/0066404). Tobin discloses the invention substantially as claimed, but fails to disclose determining the size or shape of the treatment surface of the patient using a sensor, adjusting an overall light dose with a controller based on the determined size or shape of the treatment device, or adjusting positioning of panels with at least one actuator based on the determined size or shape of the treatment device. Tapper teaches a system and method of delivering light therapy to a patient that includes an adjustable platform that is adaptable to the user's receptive surfaces (see paragraphs [0009] and [0010]). Furthermore, Tapper teaches that because users come in a variety of shapes and sizes, devices should be size or area adjustable so that the therapy can be efficiently applied and/or selectively intensified to desired treatment areas (see paragraphs [0006]). It would have been obvious to one having ordinary skill in the art before the effective filing date of the claimed invention to modify the invention of Tobin to include determining the size or shape of the treatment surface of the patient using a sensor, adjusting an overall light dose with a controller based on the determined size or shape of the treatment device, and adjusting positioning of panels with at least one actuator based on the determined size or shape of the treatment device, so that the therapy can be efficiently applied and/or selectively intensified to desired treatment areas.

35. Claims 3 and 4 are rejected under 35 U.S.C. 103 as being unpatentable over Larsen (U.S. 2005/0075703, cited above) in view of Harth et al. (U.S. 2003/0216795, cited above). Larsen discloses the invention substantially as claimed, but fails to disclose that that the illuminator is configured to output red light at an intensity of about 30 J/cm² to about 150 J/cm² or the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm². Harth teaches

a method and apparatus for providing photodynamic therapy to a patient to treat acne (see Abstract) that includes applying light using an illuminator configured to output red light at an intensity of 20 J/cm^2 , which is considered to be “about” 30 J/cm^2 (paragraph [0185], lines 5-6) and output light at an irradiance density of 10 mW/cm^2 to 30 mW/cm^2 (see paragraph [0123], lines 10-12). It would have been obvious to one having ordinary skill before effective filing date of the claimed invention to modify the invention of Larsen such that the illuminator is configured to output red light at an intensity of about 30 J/cm^2 to about 150 J/cm^2 and the illuminator is configured to output light at an irradiance density of 10 mW/cm^2 to 30 mW/cm^2 , as taught by Harth, as it has been held that combining prior art elements according to known methods to yield predictable results requires only routine skill in the art. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742, 82 USPQ2d 1385, 1396 (2007).

36. Claims 11, 12, and 14-17 are rejected under 35 U.S.C. 103 as being unpatentable over Larsen (U.S. 2005/007570, cited above) in view of Tapper et al. (U.S. 2013/0066404, cited above). Larsen discloses the invention substantially as claimed, but fails to disclose determining the size or shape of the treatment surface of the patient using a sensor, adjusting an overall light dose with a controller based on the determined size or shape of the treatment device, or adjusting positioning of panels with at least one actuator based on the determined size or shape of the treatment device. Tapper teaches a system and method of delivering light therapy to a patient that includes an adjustable platform that is adaptable to the user's receptive surfaces (see paragraphs [0009] and [0010]). Furthermore, Tapper teaches that because users come in a variety of shapes and sizes, devices should be size or area adjustable so that the therapy can be efficiently applied and/or selectively intensified to desired treatment areas (see paragraphs [0006]). It would have been obvious to one having ordinary skill in the art before the effective filing date of the claimed invention to modify the invention of Larsen to include determining the size or shape of the treatment surface of the patient using a sensor, adjusting an overall light dose with

a controller based on the determined size or shape of the treatment device, and adjusting positioning of panels with at least one actuator based on the determined size or shape of the treatment device, so that the therapy can be efficiently applied and/or selectively intensified to desired treatment areas.

37. Claim 20 is rejected under 35 U.S.C. 103 as being unpatentable over Larsen (U.S. 2005/007570, cited above). Larsen discloses the invention substantially as claimed, but fails to disclose the illuminator comprises at least three first panels having first widths, at least two second panels having second widths, wherein each of the second widths of the at least two second panels is narrower than each of the first widths of the at least three first panels; and wherein the at least three first panels and the at least two second panels are connected in an alternative manner such that each of the at least two second panels has a first lateral side connected to a respective one of the at least three first panels and a second lateral side connected to another respective one of the at least three first panels. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the invention of Larsen such that the first, third, and fifth panels shown in Figure 1 have a first width larger than the widths of the second and fourth panels in Figure 1, since it has been held that where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device, and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), cert. denied, 469 U.S. 830, 225 USPQ 232 (1984). Furthermore, it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In *re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Conclusion

38. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMMIE K MARLEN whose telephone number is (571)272-1986. The examiner can normally be reached Monday through Friday from 8 am until 4 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on 571-272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TAMMIE K MARLEN/
Primary Examiner, Art Unit 3792

<i>Notice of References Cited</i>	Application/Control No. 16/791,004		Applicant(s)/Patent Under Reexamination Boyajian et al.	
	Examiner TAMMIE K MARLEN		Art Unit 3792	Page 1 of 1

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*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
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*	B	US-20030216795-A1	11-2003	Harth, Yoram	A61N5/062	607/88
	C					
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*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

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*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	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.

<i>Search Notes</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

CPC - Searched*		
Symbol	Date	Examiner
A61N 5/06,062,0616	10/20/2021	TKM
A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662	10/20/2021	TKM
A61B5/0064,0082	10/20/2021	TKM

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name search	10/20/2021	TKM
Text-limited and related application search – see search history printout	10/20/2021	TKM
Consulted Alyssa Alter	10/20/2021	TKM

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: June 18, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3600
Examiner Name	CENTRAL, DOCKET		
Attorney Docket Number	067286-0410		
Sheet	1	of	2

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	G3	2019/0290763-A1	09-26-2019	LUNDAHL ET AL.	
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		Serial Number-Kind Code ² (if known)			

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	G6	DE-69827286-T2	11-10-2005	VIRULITE LTD [GB]		ABS
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: June 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3600
				Examiner Name	CENTRAL, DOCKET
Sheet	2	of	2	Attorney Docket Number	067286-0410

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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 ⁶
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 13, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3600
Examiner Name	CENTRAL, DOCKET				
Attorney Docket Number	067286-0410				
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 1, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3600
Examiner Name	HOLDING, DOCKET		
Attorney Docket Number	067286-0410		
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	E11	USPTO Notice of Allowance, 16/438,702 (067286-0405), 03/22/2021, 14 pages	
	E12	USPTO Office Action, Serial No. 17/009,871 (067286-0411), 03/23/2021, 9 pages	
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 19, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET				
Attorney Docket Number	067286-0410				
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		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

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	I3	USPTO Notice of Allowance, 17/009,871 (067286-0411), 7/22/2021, 14 pages	
	I4	USPTO Notice of Allowance, 17/109,311 (067286-0419), 08/10/2021, 14 pages	
	I5	USPTO Office Action, 17/109,311 (067286-0419), 07/20/2021, 17 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: January 4, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3700
Examiner Name	FRISTOE JR, JOHN K		
Attorney Docket Number	067286-0410		
Sheet	1	of	1

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		Number-Kind Code ² (if known)			
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		Serial Number-Kind Code ² (if known)			
	D3	17/109,311	12-02-2020	LUNDAHL ET AL.	

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		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

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 ⁶
	D4	USPTO Office Action, 17/009,871 (067286-0411), 12/02/2020, 15 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: July 9, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	OPAP
Examiner Name	CENTRAL, DOCKET		
Attorney Docket Number	067286-0410		
Sheet	1	of	1

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶

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 ⁶
	H1	Britannica, The Editors of Encyclopaedia, "Gel: Physics and Chemistry", 4 pages, July 20, 1998, and "Gel: Additional Information", 1 page, Available on line at: https://www.britannica.com/science/gel and https://www.britannica.com/science/gel/additional-info#history	
	H2	FEHR ET AL., Photodynamic Therapy of Vulvar and Vaginal Condyloma and Intraepithelial Neoplasia Using Topically Applied 5-Aminolevulinic Acid, Lasers in Surgery and Medicine, 2002, 30:273-279, 7 pages	
	H3	FEHR ET AL., Selective Photosensitizer Distribution in Vulvar Condyloma Acuminatum After Topical Application of 5-Aminolevulinic Acid, Am. J. Obstet. Gynecol., Volume 174(3), March 1996, pages 951-957	
	H4	HURLIMANN ET AL., Photodynamic Therapy of Superficial Basal Cell Carcinomas Using Topical 5-Aminolevulinic Acid in a Nanocolloid Lotion, Pharmacology and Treatment, Dermatology 197, 1998, pages 248-254	
	H5	REINHOLD ET AL., A Randomized, Double-Blind, Phase III, Multicentre Study to Evaluate the Safety and Efficacy of BF-200 ALA (Ameluz®) vs. Placebo in the Field-Directed Treatment of Mild-to-Moderate Actinic Keratosis with Photodynamic Therapy (PDT) When Using the BF-RhodoLED® Lamp, British Journal of Dermatology, 175(4): 696-705, February 27, 2016, 10 pages	
	H6	Third Party Submission filed in Application No. 17/109,311, June 21, 2021, 21 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 12, 2020 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3700
Examiner Name	FRISTOE JR, JOHN K		
Attorney Docket Number	067286-0410		
Sheet	1	of	1

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)			
	C1	10,357,567-B1	07-23-2019	LUNDAHL ET AL.	
	C2	2004/0010299-A1	01-15-2004	TOLKOFF ET AL.	
	C3	2009/0324727-A1	12-31-2009	FOGUET ROCA	
	C4	2011/0053965-A1	03-03-2011	TRIGIANTE, GIUSEPPE	
	C5	2014/0010761-A1	01-09-2014	PARENT ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

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 ⁶
	C6	USPTO Office Action, 16/438,702 (067286-0405), 10/13/2020, 17 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 7, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	Unassigned				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	B1	Letter to UVBiotek, LLC, dated July 28, 2017, Re: K170187, Trade/Device Name: Photodynamic Therapy Device, available at https://www.accessdata.fda.gov/cdrh_docs/pdf17/K170187.pdf (accessed April 30, 2020)	
	B2	Webpage printout, Hill Laboratories Company, "Aklarus Phototherapy Treatment System with Red, Blue and Infrared Wavelengths by Hill Therapeutics," available at https://hilllabs.com/therapeutics/Aklarus-Photo-Therapy-System.php (accessed April 30, 2020)	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	31	((("DUSA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	USPAT	OR	ON	2019/03/25 10:32
S2	30	((("BOYAJIAN") near3 ("Thomas")) OR ((("CAROTA") near3 ("Mark")) OR ((("MAZEJKA") near3 ("Brian")))).INV.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2019/03/25 10:32
S3	6	("0000002" "0000003" "0000004" "0000005" "0000006" "0000007").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 10:34
S6	4	("0000001" "0000002" "0000003" "0000004").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 10:34
S7	14	("0000001" "0000002" "0000003" "0000004" "20040162596" "20040260365" "5814008" "5849027" "9108045" "20050075703" "20060241726" "0000005" "0000006" "0000007").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 10:34
S8	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 10:37
S9	3	("0000002" "20050075703" "20060241726").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 13:09
S10	9	((("20030088296") or ("20050090877") or ("20060253175") or ("20070283655") or ("20100010591") or ("20110106222") or ("20140067024") or ("9533170"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/25 13:12
S11	6	("0000002" "20040162596" "20040260365" "5814008" "5849027" "9108045").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 13:13
S12	14	(US-0162109-\$ US-0287671-\$ US-0287696-\$ US-20060287696-\$ US-20120287671-\$ US-20150162109-\$ US-7156865-\$).DID.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 13:16

S13	3	((("20080031924") or ("20100174223") or ("20150238776"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/25 13:18
S14	2	((("20160166846") or ("20130190845"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/25 13:19
S15	12	"2007112427"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 14:58
S16	5	"38541884".FMID.	US-PGPUB; USPAT; FPRS	OR	ON	2019/03/25 14:58
S17	8	"2011124912"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 14:59
S18	4	"42228866".FMID.	US-PGPUB; USPAT; FPRS	OR	ON	2019/03/25 15:00
S19	6	("0000002" "0000003" "0000004" "0000005" "0000006" "0000007").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 15:01
S20	4	("0000001" "0000002" "0000003" "0000004").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 15:01
S21	14	("0000001" "0000002" "0000003" "0000004" "20040162596" "20040260365" "5814008" "5849027" "9108045" "20050075703" "20060241726" "0000005" "0000006" "0000007").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 15:01
S22	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:01
S23	3	("0000002" "20050075703" "20060241726").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 15:01
S24	9	((("20030088296") or ("20050090877") or ("20060253175")) or	US-PGPUB; USPAT;	OR	OFF	2019/03/25 15:01

		("20070283655") or ("20100010591") or ("20110106222") or ("20140067024") or ("9533170")).PN.	USOCR; EPO; JPO			
S25	6	("0000002" "20040162596" "20040260365" "5814008" "5849027" "9108045").PN.	US-PGPUB; USPAT	OR	ON	2019/03/25 15:01
S26	14	(US-0162109-\$ US-0287671-\$ US-0287696-\$ US-20060287696-\$ US-20120287671-\$ US-20150162109-\$ US-7156865-\$).DID.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:01
S27	3	((("20080031924") or ("20100174223") or ("20150238776"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/25 15:01
S28	2	((("20160166846") or ("20130190845"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/25 15:01
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S31	6,784	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S33	11,523	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S34	8,633	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S35	2,743	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/03/25 15:08

			JPO; DERWENT			
S36	6,725	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S37	572	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S38	1,341	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S39	4,107	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S40	1,289	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:08
S41	285	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:09
S42	282	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:09
S43	30,801	S31 S33 S34 S35 S36 S37 S38 S39 S40 S41 S42	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/03/25 15:09

			JPO; DERWENT			
S44	3,652	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:10
S45	31,604	S43 S44	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:10
S46	8,642	S45 and (diode led)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:10
S47	280	(S41 S37) and (S36 S39 S44 (diode led))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:18
S48	280	(S41 S37) and (S36 S39 S44 (diode led))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:18
S49	1,828	S46 and (panel\$4 hing\$6)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 15:19
S50	21	(US-20180236259-\$ or US-20170007844-\$ or US-20150134032-\$ or US-20120265275-\$ or US-20140350644-\$ or US-20120150265-\$ or US-20180015297-\$ or US-20180193660-\$ or US-20180280718-\$ or US-20070016269-\$ or US-20180345034-\$ or US-20110054573-\$ or US-20100017953-\$ or US-20160129279-\$ or US-20170231058-\$ or US-20170238401-\$ or US-20160235980-\$ or US-20180133497-\$	US-PGPUB; USPAT; FPRS	OR	ON	2019/03/25 15:35

		or US-20180008839-\$).did. or (US-9950136-\$).did. or (WO-2018067411-\$).did.				
S51	21	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$).did. or (US-9533170-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.	US-PGPUB; USPAT; FPRS; DERWENT	OR	ON	2019/03/25 16:11
S52	17	S51 and (@ad<="20151015" @rlad<="20151015" @prad<="20151015")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 16:12
S53	4	S51 not S52	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/25 16:12
S54	3	"39774377".FMID.	US-PGPUB; USPAT; FPRS	OR	ON	2019/03/25 16:18
S55	4	((("20050090877") or ("20060253175") or ("20140067024") or ("20060253175") or ("20150162109")).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2019/03/29 08:51
S56	6,786	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S57	11,526	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S58	8,637	A61N5/0616.cpc.	US-PGPUB; USPAT;	OR	ON	2019/03/29 08:56

			USOCR; FPRS; EPO; JPO; DERWENT			
S59	2,747	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S60	6,728	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S61	572	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S62	1,341	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
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S64	1,289	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S65	285	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S66	282	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR;	OR	ON	2019/03/29 08:56

			FPRS; EPO; JPO; DERWENT			
S67	30,814	S56 S57 S58 S59 S60 S61 S62 S63 S64 S65 S66	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S68	3,653	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S69	31,617	S67 S68	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S70	2,785	S69 and (panel\$4 hing\$6)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:56
S71	45	S69 and ((five fifth) with (panel\$4 hing\$6))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/03/29 08:58
S73	6,919	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S74	11,077	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S75	8,626	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/10/15 10:24

			JPO; DERWENT			
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S78	578	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S79	1,351	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S80	4,117	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S81	1,294	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S82	285	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S83	283	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/10/15 10:24

			JPO; DERWENT			
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S85	3,612	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S86	31,266	S84 S85	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S87	10	S86 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:24
S88	618	S86 and ((sens\$6 determin\$6 detect\$6) near3 (size shape))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/15 10:29
S89	6,941	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S90	11,104	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S91	8,674	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/10/31 13:34

			JPO; DERWENT			
S92	2,822	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S93	6,752	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S94	581	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S95	1,355	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S96	4,132	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S97	1,295	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S98	287	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S99	285	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/10/31 13:34

			JPO; DERWENT			
S100	30,552	S89 S90 S91 S92 S93 S94 S95 S96 S97 S98 S99	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S101	3,643	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S102	31,352	S100 S101	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S103	242	S102 and ((measur\$6) near3 (size shape))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/10/31 13:34
S104	6,943	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S105	11,105	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S106	8,678	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S107	2,825	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/11/04 11:37

			JPO; DERWENT			
S108	6,754	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S109	583	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S110	1,356	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S111	4,135	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S112	1,295	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S113	287	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S114	285	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S115	30,563	S104 S105 S106 S107 S108 S109 S110 S111 S112 S113 S114	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2019/11/04 11:37

			JPO; DERWENT			
S116	3,643	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S117	31,363	S115 S116	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S118	10	S117 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2019/11/04 11:37
S124	1	("20120283328").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2020/01/31 08:26
S125	22	(US-20070283655-\$ or US- 20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US- 20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US- 20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US- 20180015297-\$ or US-20180093107- \$).did. or (US-9533170-\$).did. or (EP- 2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US- 20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US- 20140157511-\$).did.	US-PGPUB; USPAT; FPRS; DERWENT	OR	ON	2020/11/23 13:14
S126	0	S125 and aminolevulinic	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 13:15
S127	0	S125 and ala	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 13:15

S128	13,320	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S129	4,618	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S130	2,839	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S131	4,119	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S132	733	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S133	1,645	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S134	5,449	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S135	8,056	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04

S136	4,864	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:04
S137	5,508	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S138	8,097	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S139	13,320	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S140	10,819	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S141	4,119	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S142	8,056	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S143	733	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05

S144	1,645	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S145	5,508	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S146	1,413	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S147	365	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S148	441	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S149	36,840	S138 S139 S140 S141 S142 S143 S144 S145 S146 S147 S148	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S150	4,864	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S151	37,870	S149 S150	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05

S152	46,164	S128 S129 S130 S131 S132 S133 S134 S135 S136 S137 S151	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:05
S153	845	S152 and \$2aminolevulinic	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/23 15:07
S154	13,321	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S155	4,619	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S156	2,842	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S157	4,120	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S158	733	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S159	1,645	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15

S160	5,449	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S161	8,057	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S162	4,865	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S163	5,509	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S164	8,098	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S165	13,321	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S166	10,819	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S167	4,120	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15

S168	8,057	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S169	733	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S170	1,645	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S171	5,509	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S172	1,413	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S173	365	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S174	441	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S175	36,843	S164 S165 S166 S167 S168 S169 S170 S171 S172 S173 S174	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15

S176	4,865	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S177	37,873	S175 S176	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S178	46,171	S154 S155 S156 S157 S158 S159 S160 S161 S162 S163 S177	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S179	845	S178 and \$2aminolevulinic	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/24 06:15
S180	1	(10/466734).APP.	USPAT; USOCR	OR	ON	2020/11/24 13:51
S181	12	"19912039".FMID.	US-PGPUB; USPAT; FPRS; JPO	OR	ON	2020/11/24 13:58
S182	39	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").PN.	US-PGPUB; USPAT	OR	ON	2020/11/24 14:10
S183	25	(US-20070283655-\$ or US- 20130066405-\$ or US-20160175609-\$ or US-20160175610-\$ or US-	US-PGPUB; USPAT;	OR	ON	2020/11/27 13:52

		20120287671-\$ or US-20060241726-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$).did. or (US-9227082-\$ or US-9017391-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.	FPRS; DERWENT			
S184	56	(US-0010591-\$ US-0031924-\$ US-0066405-\$ US-0067024-\$ US-0075703-\$ US-0088296-\$ US-0090877-\$ US-0106222-\$ US-0162109-\$ US-0162596-\$ US-0166846-\$ US-0174223-\$ US-0175609-\$ US-0175610-\$ US-0190845-\$ US-0238776-\$ US-0241726-\$ US-0253175-\$ US-0260365-\$ US-0283328-\$ US-0283655-\$ US-0287671-\$ US-0287696-\$ US-16787667-\$ US-20030088296-\$ US-20040162596-\$ US-20040260365-\$ US-20050075703-\$ US-20050090877-\$ US-20060241726-\$ US-20060253175-\$ US-20060287696-\$ US-20070283655-\$ US-20080031924-\$ US-20100010591-\$ US-20100174223-\$ US-20110106222-\$ US-20120283328-\$ US-20120287671-\$ US-20130066405-\$ US-20130190845-\$ US-20140067024-\$ US-20150162109-\$ US-20150238776-\$ US-20160166846-\$ US-20160175609-\$ US-20160175610-\$ US-5814008-\$ US-5849027-\$ US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$ US-9533170-\$).DID.	US-PGPUB; USPAT	OR	ON	2020/11/27 13:55
S185	6	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761").PN.	US-PGPUB; USPAT	OR	ON	2020/11/27 13:59
S186	1	("10357567").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2020/11/27 13:59

S187	18	S183 not (S184 S185 S186)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2020/11/27 13:59
S188	13,760	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S189	4,832	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S190	3,002	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S191	4,465	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S192	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S193	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S194	5,775	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49

S195	8,317	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S196	5,142	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S197	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S198	8,407	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S199	13,760	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S200	11,191	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S201	4,465	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S202	8,317	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49

S203	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S204	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S205	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S206	1,441	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S207	391	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S208	463	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S209	38,191	S198 S199 S200 S201 S202 S203 S204 S205 S206 S207 S208	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S210	5,142	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49

S211	39,273	S209 S210	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S212	47,948	S188 S189 S190 S191 S192 S193 S194 S195 S196 S197 S211	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S213	987	S212 and hinge	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:49
S214	23	S212 and (((wide\$4 and narrow\$6) or (first and second)) adj width)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:50
S215	117	S212 and (((wide\$4 and narrow\$6) or (first and second)) near3 width)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 12:51
S216	13,760	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S217	4,832	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S218	3,002	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44

S219	4,465	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S220	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S221	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S222	5,775	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S223	8,317	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S224	5,142	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S225	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S226	8,407	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44

S227	13,760	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S228	11,191	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S229	4,465	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S230	8,317	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S231	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S232	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S233	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S234	1,441	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44

S235	391	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S236	463	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S237	38,191	S226 S227 S228 S229 S230 S231 S232 S233 S234 S235 S236	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S238	5,142	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S239	39,273	S237 S238	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S240	47,948	S216 S217 S218 S219 S220 S221 S222 S223 S224 S225 S239	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S241	199	S240 and (((wide\$4 and narrow\$6) or (first and second)) near6 width)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/16 15:44
S242	13,763	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35

S243	4,833	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S244	3,005	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S245	4,468	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S246	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S247	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S248	5,776	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S249	8,318	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S250	5,144	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35

S251	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S252	8,408	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S253	13,763	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S254	11,195	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S255	4,468	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S256	8,318	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S257	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S258	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35

S259	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S260	1,441	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S261	391	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S262	463	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S263	38,197	S252 S253 S254 S255 S256 S257 S258 S259 S260 S261 S262	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S264	5,144	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S265	39,279	S263 S264	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S266	47,959	S242 S243 S244 S245 S246 S247 S248 S249 S250 S251 S265	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35

S267	199	S266 and (((wide\$4 and narrow\$6) or (first and second))) near6 width)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 09:35
S268	13,763	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S269	4,833	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S270	3,005	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S271	4,468	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S272	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S273	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S274	5,776	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28

S275	8,318	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S276	5,144	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S277	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S278	8,408	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S279	13,763	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S280	11,195	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S281	4,468	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S282	8,318	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28

S283	757	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S284	1,715	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S285	5,842	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S286	1,441	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S287	391	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S288	463	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S289	38,197	S278 S279 S280 S281 S282 S283 S284 S285 S286 S287 S288	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S290	5,144	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28

S291	39,279	S289 S290	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S292	47,959	S268 S269 S270 S271 S272 S273 S274 S275 S276 S277 S291	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/03/18 20:28
S293	0	2007/112427	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 13:22
S294	582,470	(stephen tobin).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 13:23
S295	242	(stephen and tobin).in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 13:23
S296	10	("0000001" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238").PN.	US-PGPUB; USPAT	OR	ON	2021/07/07 15:13
S297	2	("0000002" "D000001").PN.	US-PGPUB; USPAT	OR	ON	2021/07/07 15:13
S298	3	("0000001" "0000002" "7730893").PN.	US-PGPUB; USPAT	OR	ON	2021/07/07 15:13
S299	10	("5032400" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238").PN.	US-PGPUB; USPAT	OR	ON	2021/07/07 15:14
S300	1	("20110224598").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2021/07/07 15:15

S301	3	("0000001" "7033381" "7730893").PN.	US-PGPUB; USPAT	OR	ON	2021/07/07 15:16
S302	14	S299 S300 S301	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:16
S303	9	S302 and (wid\$6)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:18
S304	13,949	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S305	4,963	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S306	3,093	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S307	4,694	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S308	785	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S309	1,739	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/07/07 15:19

			JPO; DERWENT			
S310	5,920	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S311	8,474	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S312	5,338	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S313	6,023	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S314	8,498	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S315	13,949	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S316	11,425	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S317	4,694	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/07/07 15:19

			JPO; DERWENT			
S318	8,474	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S319	785	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S320	1,739	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S321	6,023	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S322	1,468	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S323	399	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S324	469	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S325	38,854	S314 S315 S316 S317 S318 S319 S320 S321 S322 S323 S324	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/07/07 15:19

			JPO; DERWENT			
S326	5,338	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S327	39,953	S325 S326	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S328	48,853	S304 S305 S306 S307 S308 S309 S310 S311 S312 S313 S327	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:19
S329	217	S328 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/07/07 15:21
S331	3	("0000001" "0000002" "20200100997").PN.	US-PGPUB; USPAT	OR	ON	2021/08/26 12:36
S332	2	((("20160346392") or ("20200100997"))).PN.	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	OFF	2021/08/26 12:37
S333	14,216	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S334	5,141	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S335	3,204	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/08/26 12:42

			JPO; DERWENT			
S336	4,914	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S337	808	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S338	1,778	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S339	6,128	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S340	8,649	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S341	5,526	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S342	6,224	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S343	8,694	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/08/26 12:42

			JPO; DERWENT			
S344	14,216	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S345	11,742	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S346	4,914	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S347	8,649	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S348	808	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S349	1,778	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S350	6,224	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S351	1,481	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/08/26 12:42

			JPO; DERWENT			
S352	408	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S353	492	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S354	39,744	S343 S344 S345 S346 S347 S348 S349 S350 S351 S352 S353	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S355	5,526	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S356	40,873	S354 S355	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S357	50,063	S333 S334 S335 S336 S337 S338 S339 S340 S341 S342 S356	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S358	222	S357 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/08/26 12:42
S360	37	((("DUSA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	USPAT	OR	ON	2021/10/18 15:52

S361	38	((("BOYAJIAN") near3 ("Thomas"))) OR (("CAROTA") near3 ("Mark")) OR (("MAZEJKA") near3 ("Brian"))).INV.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:52
S362	64	("0000002" "0000011" "20200100997" "0000001" "20190290763" "20200269063" "20200398071" "7730893" "20090247932" "20110224598" "20130274834" "20130289089" "20150290028" "20160008623" "20200261580" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238" "0017109" "20010021812" "D000001" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").PN.	US-PGPUB; USPAT	OR	ON	2021/10/18 15:52
S363	14,281	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S364	5,189	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S365	3,246	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/10/18 15:53

			JPO; DERWENT			
S366	4,993	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S367	815	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S368	1,794	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S369	6,171	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S370	8,713	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S371	5,588	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S372	6,285	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S373	8,738	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/10/18 15:53

			JPO; DERWENT			
S374	14,281	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S375	11,844	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S376	4,993	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S377	8,713	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S378	815	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S379	1,794	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S380	6,285	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S381	1,484	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	2021/10/18 15:53

			JPO; DERWENT			
S382	413	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S383	498	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S384	39,984	S373 S374 S375 S376 S377 S378 S379 S380 S381 S382 S383	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S385	5,588	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S386	41,124	S384 S385	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S387	50,408	S363 S364 S365 S366 S367 S368 S369 S370 S371 S372 S386	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S388	3,097	S387 and (uniform\$6 with (light illuminat\$8))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:53
S389	29	(US-20070283655-\$ or US- 20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US- 20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-	US-PGPUB; USPAT; FPRS; DERWENT	OR	ON	2021/10/18 15:54

		20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.				
S390	10	S389 and (uniform\$6 with (light illuminat\$8))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/18 15:54
S391	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S392	5,241	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S393	3,302	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S394	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S395	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27

S396	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S397	6,249	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S398	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S399	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S400	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S401	8,783	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S402	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S403	11,938	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27

S404	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S405	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S406	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S407	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S408	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S409	1,489	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S410	416	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S411	512	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27

S412	40,271	S401 S402 S403 S404 S405 S406 S407 S408 S409 S410 S411	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S413	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S414	41,417	S412 S413	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S415	50,819	S391 S392 S393 S394 S395 S396 S397 S398 S399 S400 S414	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S416	15	S415 and (nest\$6 near3 hing\$9)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:27
S417	7	S415 and (recess\$6 near3 hing\$9)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:30
S418	0	S415 and (hidden near3 hing\$9)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 10:30
S419	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50

S420	5,241	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S421	3,302	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S422	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S423	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S424	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S425	6,249	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S426	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S427	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50

S428	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S429	8,783	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S430	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S431	11,938	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S432	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S433	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S434	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S435	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50

S436	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S437	1,489	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S438	416	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S439	512	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S440	40,271	S429 S430 S431 S432 S433 S434 S435 S436 S437 S438 S439	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S441	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S442	41,417	S440 S441	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S443	50,819	S419 S420 S421 S422 S423 S424 S425 S426 S427 S428 S442	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50

S444	59	S443 and (dead near3 space)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:50
S445	61	S443 and (hing\$6 with (reduce reduced reducing reduction minim\$9))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:51
S446	66	S443 and (hing\$6 with (reduce reduced reducing reduction minim\$9 decreas\$6))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:52
S447	112	S444 S445 S446	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/19 15:52
S448	30	(US-20070283655-\$ or US- 20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US- 20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US- 20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US- 20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US- 20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US- 9533170-\$ or US-9227082-\$ or US- 9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356- \$).did. or (US-20160175609-\$ or US- 20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US- 20140157511-\$ or US-20160310756- \$).did.	US-PGPUB; USPAT; FPRS; DERWENT	OR	ON	2021/10/20 13:42
S449	17	S448 and output	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:42

S450	19	S448 and (shape size measur\$6)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:45
S451	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S452	5,241	A61B5/0064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S453	3,302	A61B5/0082.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S454	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S455	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S456	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S457	6,249	A61N2005/0651.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49

S458	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S459	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S460	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S461	8,783	A61N5/06.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S462	14,390	A61N5/062.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S463	11,938	A61N5/0616.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S464	5,080	A61N2005/0626.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S465	8,785	A61N2005/0652.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49

S466	826	A61N2005/0633.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S467	1,805	A61N2005/0642.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S468	6,340	A61N2005/0663.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S469	1,489	A61N2005/0636.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S470	416	A61N2005/064.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S471	512	A61N2005/0658.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S472	40,271	S461 S462 S463 S464 S465 S466 S467 S468 S469 S470 S471	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S473	5,664	A61N2005/0662.cpc.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49

S474	41,417	S472 S473	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S475	50,819	S451 S452 S453 S454 S455 S456 S457 S458 S459 S460 S474	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S476	1,292	S475 and ((sens\$6 detect\$6) near5 (shape size))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:49
S477	45	S475 and ((sens\$6 detect\$6) with (shape size) with (treatment adj (surface area)))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:51
S478	54	S475 and ((sens\$6 detect\$6 measur\$6) with (shape size) with (treatment adj (surface area)))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:54
S479	162	S475 and ((sens\$6 detect\$6 measur\$6 adjust adjusting adjusted adjustable "based on") with (shape size) with (treatment adj (surface area)))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:58
S480	88	S479 and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 13:59
S481	17	S448 and ("j/cm" "mw/cm" nm nanometer)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:47

S482	0	S448 and ("j/cm" "mw/cm")	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:47
S483	7	S475 and ("j/cm" "mw/cm" nm nanometer)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2021/10/20 15:47
S484	46	S475 and ("j/cm" "mw/cm" (nm or nanometer))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	ON	2021/10/20 15:48
S485	34	S484 and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:48
S486	629	S475 and (intensity with red) and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:52
S487	442	S475 and (intensity with red with light) and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:52
S488	0	S475 and (intensity with red with "j/cm") and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:53
S489	7	S475 and (intensity with "j/cm") and @ad<="20151015"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2021/10/20 15:53

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S119	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	US-PGPUB; USPAT	OR	ON	2019/11/04 11:19
S120	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	US-PGPUB; USPAT	OR	ON	2019/11/04 11:20
S121	189	(panel AND width AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	US-PGPUB; USPAT	OR	ON	2019/11/04 11:23
S122	213	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	US-PGPUB; USPAT	OR	ON	2019/11/04 11:23
S123	3	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))).clm.	US-PGPUB; USPAT	OR	ON	2019/11/04 11:38
S330	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	US-PGPUB; USPAT	OR	ON	2021/07/07 19:14
S359	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	US-PGPUB; USPAT	OR	ON	2021/08/26 12:42

10/20/2021 6:57:03 PM

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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	Unassigned
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	Unassigned
Examiner Name	Unassigned				
Sheet	1	of	3	Attorney Docket Number	067286-0410

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
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	A22	2008/0031924-A1	02-07-2008	GILSON ET AL.	
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	A33	2016/0166846-A1	06-16-2016	CHAE, HIUN SUK	
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Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known	
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				First Named Inventor	Thomas BOYAJIAN
				Art Unit	Unassigned
Examiner Name	Unassigned				
Sheet	2	of	3	Attorney Docket Number	067286-0410

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
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	A37	WO-02/13788-A1	02-21-2002	GEN HOSPITAL CORP		
	A38	WO-2007/112427-A2	10-04-2007	TOBIN, STEPHEN M.		
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	A40	WO-2011/124912-A1	10-13-2011	DOUGAL, GORDON REX, PATTERSON		
	A41	WO-2014/131115-A1	09-04-2014	KLOX TECHNOLOGIES INC [CA]		ABS
	A42	WO-2015/041919-A1	03-26-2015	D-REV: DESIGN FOR THE OTHER NINETY PERCENT		
	A43	WO-99/22802-A1	05-14-1999	DUSA PHARMACEUTICALS INC [CA]		

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 ⁶
	A44	Australian Office Action, Application No. 2019200152, 11/11/2019, 9 pages	
	A45	European Office Action, Application No. 16787667.1, 9/24/2019, 5 pages	
	A46	GLAD.com.au: "GLAD History", 2012, [online] URL: http://www.glad.com.au/about-glad/glad-history/ , retrieved online 8 November 2019	
	A47	International Preliminary Report on Patentability, PCT/US2016/056572, April 26, 2018, 9 pages	
	A48	International Preliminary Report on Patentability, PCT/US2018/027070, 10/24/2019, 10 pages	
	A49	Notice of Allowance, 15/487,991 (067286-0398), 01/15/2020, 11 pages	
	A50	Notice of Allowance, 15/487,991 (067286-0398), 10/02/2019, 16 pages	
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 14, 2020 <i>(use as many sheets as necessary)</i>				Complete if Known		
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				First Named Inventor	Thomas BOYAJIAN	
				Art Unit	Unassinged	
				Examiner Name	Unassinged	
Sheet	3	of	3	Attorney Docket Number		067286-0410

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	A54	USPTO Interview Summary, 15/487,991 (067286-0398), 9/22/2017, 4 pages		
	A55	USPTO Notice of Allowance, 15/292,731 (067286-0395), 11/14/2019, 12 pages		
	A56	USPTO Office Action, 15/487,991 (067286-0398), 07/31/2018, 20 pages		
	A57	USPTO Office Action, 15/487,991 (067286-0398), 04/09/2019, 27 pages		
	A58	USPTO Office Action, 15/487,991 (067286-0398), 06/12/2017, 22 pages		
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	10/19/2021
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**Courtesy Reminder for
Application Serial No: 16/791,004**

Attorney Docket No: 067286-0410

Customer Number: 22428

Date of Electronic Notification: 10/25/2021

This is a courtesy reminder that new correspondence is available for this application. If you have not done so already, please review the correspondence. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

An email notification regarding the correspondence was sent to the following email address(es) associated with your customer number:
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If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov or call 1-866-217-9197.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
				Examiner Name	MARLEN, TAMMIE K
Sheet	1	of	3	Attorney Docket Number	067286-0410

U.S. PATENT DOCUMENTS					
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		Serial Number-Kind Code ² (if known)			
	J1	17/487,698	09-28-2021	LUNDAHL ET AL.	
	J2	17/506,849	10-21-2021	BOYAJIAN ET AL.	

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		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	J3	WO-96/06602-A1	03-07-1996	NOVEN PHARMA		

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 ⁶
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		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
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	J17	Fauteck JD, Ackermann G, Birkel M, Breuer M, Moor AC, Ebeling A, Ortlund C. Fluorescence characteristics and pharmacokinetic properties of a novel self-adhesive 5-ALA patch for photodynamic therapy of actinic keratoses, 2008.	
	J18	Harris DR. Percutaneous absorption and the surface area of occluded skin: a scanning electron microscopic study. British Journal of Dermatology. 1974; 91(27-32)	
	J19	Hongcharu W., Taylor C., Chang, Y., Aghasi, D., Suthamjariya, K., Anderson, R. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. J Invest Dermatol. 2000 Aug;115(2):183-92	
	J20	International Patent Reviews, LLC review of U.S. Patent No. 10,357,567 dated July 26, 2021	
	J21	Jeffes E., McCullough J., Weinstein G., Fergin P., Nelson J., Shull T., Simpson K., Bukaty L., Hoffman W., Fong N. Photodynamic therapy of actinic keratosis with topical 5- aminolevulinic acid. A pilot dose-ranging study. Arch Dermatol. 1997	
	J22	Levulan, Label (2002)	
	J23	Levulan, Label (2009)	
	J24	MacCormack MA. Photodynamic therapy in dermatology: an update on applications and outcomes. Semin Cutan Med Surg. 2008 Mar;27(1):52-62	
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		Examiner Name	MARLEN, TAMMIE K		
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(54) Title: COMPOSITIONS AND METHODS FOR THE ADMINISTRATION OF δ -AMINOLEVULINIC ACID AND PHARMACEU- TICAL EQUIVALENTS THEREOF			
(57) Abstract <p>A pharmaceutical composition of increased stability, which comprises ALA or pharmaceutical equivalents thereof and a pharmaceutically acceptable, flexible, finite carrier suitable for administration to the skin or other dermal membrane of a mammal, optionally containing a stabilizing amount of an organic weak proton donor or saccharide containing substance. The pharmaceutically acceptable carrier in solid formulation can be a skin patch, many forms and types of which are known and used in the art. It is preferable that the composition be anhydrous. The formulations appear to improve the fluorescence produced after exposing treated skin to activating light, as compared with the fluorescence produced with ALA in a fluid carrier. In particular, the pattern of fluorescence is more even and uniform over the area of application than with topical creams or salves and may provide increased fluorescence.</p>			

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COMPOSITIONS AND METHODS FOR THE
ADMINISTRATION OF δ -AMINOLEVULINIC ACID
AND PHARMACEUTICAL EQUIVALENTS THEREOF

5 Cross-Reference to Related Applications

 This application is a continuation-in-part of
PCT/US94/09466, filed August 27, 1994, which is a
continuation-in-part of Serial No. 08/112,330 filed
August 27, 1993, which is a continuation-in-part of
10 PCT/US92/01730, filed February 27, 1992, which is a
continuation-in-part of U.S. Application Serial No.
07/813,196, filed December 23, 1991, now U.S. Patent No.
5,234,957, which is a continuation-in-part of U.S. Patent
Application Serial No. 07/661,827, filed February 27,
15 1991 and now abandoned. All of the foregoing
applications are hereby incorporated by reference.

Background of the Invention

 5-Aminolevulinic acid, also referred to as δ -
aminolevulinic acid or 5-amino-4-oxopentanoic acid, is
20 referred to herein as "ALA". ALA has been known for over
40 years to be a precursor in the metabolic pathway to
heme in humans and to chlorophyll in plants. Until the
past ten years ALA has been of limited usefulness,
namely, use limited to porphyrin research. In 1984, ALA
25 was proposed for use as a photodynamic herbicide. It has
been discovered recently that ALA can be used by various
routes of administration to detect and treat certain
conditions involving rapidly metabolizing cells, namely
hyperproliferative cells. It is especially useful in the
30 treatment of malignant and non-malignant abnormal
growths.

 ALA has been administered by various routes known for
use in drug administration, but especially by topical

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application to the skin and epithelium of various body cavities. Application of ALA results in the selective accumulation of clinically significant amounts of protoporphyrin IX, another precursor in the metabolic pathway to heme. Activation of protoporphyrin IX by light, depending on the wavelength of the light, will cause the protoporphyrin IX either to fluoresce (which can be used as the basis of a detection method), or to decompose (which can be used as the basis of treatment for cells that need to be removed).

ALA previously has been used in clinical testing on humans and other mammals in aqueous and non-aqueous fluid vehicles such as creams (oil in water emulsions) and lotions for application to the skin and orally for the diagnosis and treatment of skin cancers. ALA has been used in clinical studies in aqueous solution for application to the endometrial cavity.

ALA has been reported to inhibit degradation of the drug calcitonin by the nasal mucosa peptides in U.S. 5,026,825 . Preparations in the examples of that patent show a combination of calcitonin and ALA in aqueous solutions containing one or more of benzalkonium chloride, citric acid, sodium citrate, hydrochloric acid, sodium acetate and acetic acid. The organic acids and their salts appear to be used as buffers, to adjust the pH of the resulting solution to about 4.

ALA has a tendency to decompose in a wide variety of vehicles used in clinical testing including both water containing vehicles, anhydrous fluid vehicles and water and oil emulsions. In general, the lower the pH of the fluid vehicle, the more rapid the degradation. For example, addition of about 10% by weight ALA in the form the hydrochloride salt into an alkaline solution, left at room temperature, results in almost complete degradation in about one week.

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Precursors or prodrugs of ALA have been reported for use in conditions similar to that as reported for ALA. The Norwegian Radium Hospital Research Foundation's PCT application No. WO 95/07077 published March 16, 1995 ("precursors") and Peng et al. Abstract, American Society of Photobiology Annual Meeting, 1995 Budapest.

The decomposition occurring with fluid preparations, such as water and ethanol, reported in the scientific literature with use of ALA patients, is sufficient to preclude the use of ALA in a product to be distributed in normal, existing channels for the supply of pharmaceuticals. Many studies have been performed without success in an attempt to stabilize ALA, with respect to extending the stability of the chemical in a fluid, including use of an aqueous solution containing certain antioxidants such as ascorbic acid and sodium bisulfite. Thus, there remains a need for a storage stable composition comprising ALA in a form suitable for administration to a patient.

Summary of the Invention

The invention relates to a pharmaceutical composition of increased stability, which comprises ALA and a pharmaceutically acceptable, flexible, finite carrier suitable for administration to the skin or other dermal membrane of a mammal, optionally containing a stabilizing amount of an organic weak proton donor or a saccharide.

The pharmaceutically acceptable carrier in solid formulation for topical delivery to the skin is desirably a skin patch, many forms and types of which are known and used in the art. It is preferable that the composition be prepared without - and essentially contain no - water. Not only are these formulations using a topical solid carrier stable after prolonged storage, but use of the formulations appear to improve the fluorescence produced

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after exposing treated skin to activating light, as compared with the fluorescence produced with ALA in a fluid carrier. In particular, the pattern of fluorescence is more even and uniform over the area of application than with topical creams or salves, and may even provide increased fluorescence.

When preparing the solid formulations for topical administration, addition of a proton donor, such as a weak organic acid, can be used to increase the long-term stability of the patch. Suitable organic acids are mono- and polycarboxylic acids such as citric acid, oxalic and ascorbic acids. Weak organic acids are preferred because they are less irritating and less likely to affect the stability of the ALA. The additive also can be a saccharide. If the solid preparation contains water, it is essential to include the stabilizing amount of a proton donor or saccharide-containing substance. Anhydrous preparations, however, are preferred.

The term "stabilizing amount," when applied to the mild organic proton donor or the saccharide-containing substance of the present invention, means a concentration sufficient to prevent or minimize the degradation of ALA over the expected storage time for the composition, typically 6 months to two years. In general, this amount should be an amount at least equal in weight to the ALA present, although concentrations as high as four times the weight of ALA can be used. The saccharide-containing substance can be a complex saccharide such as starch, a gum or a polysaccharide or it can be less complex saccharide such as a monosaccharide.

The mechanism by which the solid topical formulation stabilizes the ALA is unknown. The mechanism by which the weak organic proton donor such as the weak organic acid or the saccharide-containing substance increases the stability of ALA also is unknown. It cannot be explained

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merely as a reducing effect which prevents the oxidation of ALA, since other anti-oxidants, such as Vitamin E, BHT, BHA, ascorbic acid and sodium bisulfite used in an aqueous solution, were not found to be effective at
5 increasing the stability of ALA. It is unknown whether this effect is one of protection by the saccharide-containing substance of the degradation sites on the ALA.

This invention also comprises the method of stabilizing ALA by mixing the same with an anhydrous,
10 flexible, finite, pharmaceutically acceptable carrier for topical administration. The carrier also may comprise a weak organic proton donor or saccharide, a solid polymer, or two or more of the foregoing.

Detailed Description of the Preferred Embodiments

15 It now has been found that ALA can be prepared in a stable formulation for topical use by incorporation into a topical drug delivery carrier, optionally containing a mild organic proton donor or saccharide containing substance. In a preferred embodiment, the delivery
20 carrier is contained in a patch. Use of topically acting ALA in a patch is unusual since, because of the increased costs associated with manufacture of patches. Typically, because of these costs, patches are used only for prescription drugs intended for systemic effect, but
25 which are given topically to avoid degradation by the liver or to prolong the rate and extent of distribution.

The term a δ -aminolevulinic acid as used herein refers to ALA, pharmaceutically acceptable salts thereof and prodrugs, which are considered pharmaceutical
30 equivalents for purposes of this invention. The nature of such salts and prodrugs are known to skilled workers in the arts. The pharmaceutically acceptable salts include, but are not limited to, acid addition salts with inorganic and organic acids as well as quaternary

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ammonium salts of ALA. Suitable inorganic salts include hydrochloride, hydrobromide, sulfate, carbonate, hydrogen carbonate, hydrogen sulfate and like inorganic salts known for use with pharmacologically active substances.

5 Suitable organic acids are those mono- and polycarboxylic acids such as citric acid, ascorbic acid, oxalic acid and benzoic acid which are weak acids and can also act as a proton donor. A suitable quaternary ammonium salt is

10 olealkonium chloride and other quaternary ammonium salts that are generally recognized as safe and effective ("GRAS") under the food and drug laws for application to dermal membranes. See generally Bundgaard, H. (ed.) cited below.

15 The other pharmaceutically acceptable prodrugs of ALA include the pharmaceutically acceptable esters - amides and other masked forms or derivatives thereof - that are metabolized *in vivo* to yield ALA or a solubilized form thereof.

20 Because of the instability of ALA in a strongly acidic milieu, esterification of ALA with an aliphatic alcohol, which is normally catalyzed by a strong acid, is not preferred. Esterification may, however, be accomplished by an alternate route. For example, the

25 amino group is protected by a carbobenzoxy group by reaction with carbobenzoxy succinimide. The CBZ-ALA is reacted with a diazoalkane such as diazomethane to produce CBZ-ALA ester. The CBZ group is then removed by hydrogenolysis to produce an ALA carboxylic acid ester. The yields by such a procedure are virtually

30 quantitative.

35 "Pharmaceutically acceptable ester" refers to those esters which retain, upon hydrolysis of the ester bond *in vivo*, the biological effectiveness and properties of the carboxylic acid and are not biologically or otherwise undesirable. For a description of pharmaceutically

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acceptable esters as prodrugs, see Bundgaard, H., ed., (1985) Design of Prodrugs, Elsevier Science Publishers, Amsterdam. Generally, ester formation can be accomplished via conventional synthetic techniques.

5 (See, e.g., March Advanced Organic Chemistry, 3rd Ed., John Wiley & Sons, New York (1985) p. 1157 and references cited therein, and Mark et al., Encyclopedia of Chemical Technology, John Wiley & sons, New York (1980).) The ester component of the carboxylic acid ester will

10 generally comprise (i) a C1-C22 alkane that can also contain one or more double bonds and can contain branched carbon chains or (ii) a C7-C12 aromatic or heteroaromatic group. This invention also contemplates the use of those compositions which are both esters as described herein

15 and at the same time are the pharmaceutically acceptable acid addition salts thereof.

"Pharmaceutically acceptable amide" refers to those amides which retain, upon hydrolysis of the amide bond, the biological effectiveness and properties of the

20 carboxylic acid or amine and are not biologically or otherwise undesirable. For a description of pharmaceutically acceptable amides as prodrugs, see Bundgaard, H., ed., (1985) Design of Prodrugs, Elsevier Science Publishers, Amsterdam. These amides are

25 typically formed from the corresponding carboxylic acid and an amine. Generally, amide formation can be accomplished via conventional synthetic techniques. (See e.g., March Advanced Organic Chemistry, 3rd Ed., John Wiley & Sons, New York (1985) p. 1152, and Mark et al.,

30 Encyclopedia of Chemical Technology, John Wiley & Sons, New York (1980).) This invention also contemplates the use of those compositions which are both amides as described herein and at the same time are the pharmaceutically acceptable acid addition salts thereof.

35 The stability of ALA may be increased by incorporating it into a solid, pharmaceutically

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acceptable carrier, preferably a topical carrier and more preferably in an anhydrous adhesive topical carrier. The solid carrier can optionally contain an organic weak proton donor such as a weak organic acid, or a
5 saccharide-containing substance.

The term "pharmaceutically acceptable carrier" used here with reference to topical administration refers to the wide variety of carriers known for use for application to the skin or body cavity to a dermal
10 membrane. Such carriers are well known in the art.

The term "organic weak proton donor" used here refers to an organic substance known to function as a weak acid which does not, at the same time, degrade the ALA. Whether the organic substance will degrade the ALA can be
15 determined easily by placing the substance at the concentration intended for use with the ALA, then analyzing for residual ALA. Suitable organic weak proton donors are organic weak acids such as mono- and polycarboxylic acids such as citric acid, oxalic acid,
20 ascorbic acid and benzoic acid. Other suitable stabilizers are gums such as guar gum, xanthan gum, karaya gum, British gum, starch gum, tragacanth gum, pectin gum and derivatives thereof, saccharides such as complex saccharides such as cellulose, polysaccharides
25 such as dextran and dextrin, and monosaccharides such as dextrose, fructose, maltose, D-glucose and L-glucose. Corn syrup, composed of dextrin and glucose is particularly useful, but its use is limited by the fact that it generally contains water.

30 The solid topical forms of the present invention include all the known types of devices, including both the adhesive matrix and reservoir devices. Matrix devices are preferred because the minimization of the number of layers of the device results in ease of
35 preparation. The matrix devices are prepared by methods

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known in the art. The most convenient form for manufacture of a matrix device is one in which the ALA is dispersed in a pressure sensitive adhesive. The matrix devices are preferably prepared using commercially supplied organic solvents containing the polymer. The additional ingredients are added to the mixture and then the solvents are removed to form the patch. This avoids the use of or inclusion of water in the composition and the need to perform a cross-linking step after the mixing, such as is necessary for emulsion polymerization.

Pressure sensitive adhesives useful in preparing the preferred topical compositions include a wide variety of polymeric adhesives including pharmaceutically acceptable acrylics, vinyl acetate, silicone and synthetic or natural rubber adhesives and mixtures thereof. Acrylic adhesives include Gelva adhesives GMS 1430, 788 available from Monsanto Co. and various Durotak adhesives such as 87-2852 manufactured by National Starch. Vinylacetate adhesives including Flexbond 149 and 150 from Air Products are of limited usefulness because they contain water. Rubber based adhesives such as the Morstiks from Morton Thiokol, Ins. or Vistanex manufactured by Exxon Chemicals can be used. Numerous silicone based adhesives are available from Dow-Corning. These and other pressure sensitive adhesives suitable for topical application will be apparent to one skilled in the art.

For adhesive matrix devices, the polymer blend is applied to a suitable backing material impermeable to the drug or the other components of the polymer matrix. The backing materials, which are preferably water resistant, and occlusive or non-occlusive, can be selected from such material as foam, metal foil, polyester, low density polyethylene, copolymers of vinyl chloride and polyvinylidene chloride and laminates thereof.

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Where the topical device is a reservoir-type device, the ALA in a solvent, preferably in a non-aqueous solvent such as an alkanediol or an organic acid such as citric acid is used to fill the reservoir. About 0.1 to about 2%, preferably about 0.5% of a gelling agent such as hydroxypropyl cellulose, can be added to form a gel. The solution or gel is retained in the reservoir by a suitable rate-controlling membrane such as an ethylene-vinyl acetate copolymer membrane, which membrane preferably has a face layer of a pressure sensitive adhesive as described above. Backing materials are similar to those described above for matrix devices.

Both adhesive matrix and reservoir devices contain a release liner impermeable to the drug and any solvents present in the system in order to protect the adhesive layer until the patch is to be applied to the skin. Typical materials for release liners are polyester, polyethylene, and polyethylene coated paper, preferably silicon-coated to facilitate removal.

The adhesive matrices of the present invention contain 0.5 to 50% ALA by weight, preferably 5 to 20%, and most preferably 10 to 20%; 50 to 95% adhesive, preferably 60 to 90% and more preferably 70 to 90%. An optional carrier and may contain from 0 to 40% by weight of other components, such as a proton donor, penetration enhancer and other substances known for use in transdermal formulations. Since the ALA in the solid formulation is used for a topical effect, there is in fact no maximum limitation as to the amount of ALA that can be used in the patch except to the extent that the adhesiveness or stability of the patch is affected.

Methods for preparing adhesive matrix devices are known in the art. A preferred method for preparing adhesive matrix topical devices of the present invention comprises coating a thin layer of the adhesive polymer

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containing the ALA optionally in an anhydrous solvent and optionally containing a mild organic proton donor such as saccharide-containing substance or a mild organic acid onto the material to be used as a release liner, cross-
5 linking the polymer blend in the case of an adhesive to be cross-linked, drying the release liner containing the polymer mixture, then laminating the backing material to the resultant adhesive layer. The preferred proton donor for the ALA is any liquid material or a saccharide-
10 containing substance or an organic acid such as citric acid in a non-aqueous solvent. Additional substances which increase the passage of the drug into the skin also can be added. Suitable sized patches can then be cut out and the patches preferably sealed in protective pouches.

15 The layer of polymer mixture cast on the release liner according to the preferred method of this invention is about 5 mils to about 30 mils thick. The coated layer is preferably dried at a temperature of about 80 degrees Centigrade. One mil = 0.0254 mm.

20 The size of the topical device of the present invention depends on the dose of ALA to be utilized, with the preferred patch area being about 2.5 to 20 cm², preferably 5 to 15 cm². The preferred delivery rate for ALA is at least 0.1 µg. per cm² per hour, giving a
25 preferred daily dosage of at least 0.25 mg. per day applied to the area of the skin to be diagnosed or treated for about 2-48 hours. The optimum concentration of ALA in a patch is at least 0.1-3.0 mg. per cm².

30 As a minimum, the topical device must contain a pharmacologically effective amount of ALA. Generally, this is at least 0.25 mg. The duration of application is that period sufficient to achieve ALA penetration into the diseased tissue and that permits high localized concentrations of protoporphyrin IX resulting from the
35 conversion of ALA. This period may be about 3-24 hours

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and, preferably, is 12-16 hours. The effective amount and duration will vary depending on the nature of the lesion and may be determined empirically by those skilled in the art by testing localized fluorescence of the lesion after administration. If fluorescence is insufficient, longer application or higher ALA concentrations may be used.

Topical ALA photodynamic therapy (ALA PDT™) involves the exposure of the ALA-treated lesion with light. A suitable wavelength is 400 nm, 634 nm or 600-700 nm, at an intensity of 10-100 milliwatts per centimeter squared (mW/cm²) to provide a light dose of 10-100 Joules/cm². Exposure time may vary from 3 to 30 minutes, but preferably is about 10 minutes. Upon exposure, activation of protoporphyrin IX leads to *in situ* breakdown of protoporphyrin IX and the generation of singlet oxygen, leading to the destruction of diseased cells.

The target tissues for which the present invention may be used are any visible, cutaneous lesion or other undesired rapidly growing cells. In particular, these include, but are not limited to, neoplastic, aplastic and hyperplastic skin conditions such as basal cell carcinoma, actinic keratosis, psoriasis and similar conditions.

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Example 1

The following table shows typical adhesive matrix formulations of this invention. In this table GMS means Gelva multipolymer system, and the percentages shown are percentages by weight:

Gelva Multipolymer Solution = Acrylic Adhesive = GMS

	%w/w	%w/w	%w/w	%w/w	%w/w	%w/w	%w/w	%w/w
GMS 1430	80	90	80	70	65	80		
ALA	10	10	10	10	10	10		
Citric Acid	10	-	5	10	5	-		
Corn Syrup	-	-	5	10	20	10		
GMS 788	80	90	80	70	60	50	50	
ALA	10	10	10	10	10	10	10	
Citric Acid	10	-	5	10	-	-	10	
Corn Syrup	-	-	5	10	30	40	30	
GMS 788	40	80	70	35	30	25	25	45
GMS 1430	40	5	5	35	30	25	25	45
ALA	10	10	10	10	10	10	10	10
Citric Acid	10	5	5	10	-	-	10	-
Corn Syrup	-	-	10	10	30	40	30	-
Duro-Tak 87-2852	80	80	50	50	60	70	70	90
ALA	10	10	10	10	10	10	10	10
Citric Acid	10	-	-	10	10	5	-	-
Corn Syrup	-	10	40	30	20	15	20	-

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Example 2

In the following example the ALA, propylene glycol, lecithin and glycerin are blended at about 70 to 90°C until all the drug is dissolved. The solution is then cooled to about 20 to 35°C prior to adding the karaya gum. Once the karaya gum is added, the final composition is applied to a suitable backing material such as a non-woven polyester film (for example, the film sold under the trademark Sontara 8100, manufactured by DuPont de Nemours, Wilmington, DE) and warmed to about 100°C to accelerate the formation of the gel into its final, finite form.

5-Aminolevulinic Acid

	%w/w	%w/w	%w/w	%w/w	%w/w
ALA	2	5	10	15	20
Solvent (dipropylene glycol)	10	10	15	15	15
Solvent (Oleic acid)	10	10	10	10	10
Solvent (glycerin)	30	30	20	20	30
Solvent (isocetyl alcohol)	—	—	10	10	—
Bioadhesive (karaya gum)	30	30	20	20	30
Bioadhesive (xanthan gum)	—	—	10	10	—
Binder (lecithin)	18	15	10	10	—

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Example 3

A thirty-two year old female is diagnosed with basal cell carcinoma. A single lesion is evident on her right forearm covering approximately 22 mm², and topical aminolevulinic acid photodynamic therapy (ALA PDT™) is prescribed.

A 5 cm² topical patch containing 10% (w/w) ALA, made according to Example 1 or 2, is applied to the lesion. The patch is left in place for 18 hours, which is sufficient to permit adequate penetration of ALA into the lesion and for the formation of protoporphyrin IX ("PpIX"), the active end product of topical ALA administration. After the patch is removed, the lesion is wiped with an alcohol swab to remove any residual adhesive.

The lesion is then exposed to activating UV light using a conventional Woods lamp to determine if the fluorescence levels, and hence the PpIX levels, are sufficient. Finding the levels suitable, the lesion is then exposed to a 634 nm wavelength light source at 100 mW/cm² for 15 minutes.

Within 30 minutes, a localized reaction is observed, characterized by the rapid onset of redness, erythema and edema at the treatment site. During the next several days, necrosis of the destroyed lesional cells ensues, resulting in the formation of a burn-like scab over the former lesion. During the next six weeks, normal healing of the treated tissue and restoration of intact skin is observed.

The foregoing examples are illustrative embodiments of the invention and are merely exemplary. A person skilled in the art may make variations and modification without departing from the spirit and scope of the

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invention. All such modifications and variations are intended to be included within the scope of the invention as described in this specification and the appended claims.

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What Is Claimed Is

1. A pharmaceutical composition comprising:
 - (i) a therapeutically effective amount of a δ -aminolevulinic acid or a pharmaceutical equivalent thereof; and
 - (ii) a pharmaceutically acceptable, flexible, finite carrier for dermal application.
2. The composition of claim 1, wherein said pharmaceutical equivalent is an ester of δ -aminolevulinic acid.
3. The composition of claim 1, wherein said pharmaceutical equivalent is an amide of δ -aminolevulinic acid.
4. The pharmaceutical composition of claim 1, wherein said δ -aminolevulinic acid or pharmaceutical equivalent thereof is dispersed throughout the carrier.
5. The pharmaceutical composition of claim 1, wherein said carrier is an adhesive.
6. The pharmaceutical composition of claim 5, wherein said adhesive is a pressure-sensitive adhesive.
7. The pharmaceutical composition of claim 6, wherein said pressure sensitive adhesive is a bio-adhesive.
8. The pharmaceutical composition of claim 6, wherein said pressure sensitive adhesive is a polymeric adhesive selected from the group consisting of an acrylic, a silicone-based adhesive, a vinyl acetate adhesive and a natural or synthetic rubber-based adhesive, or mixtures thereof.

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9. The pharmaceutical composition of claim 5, wherein said adhesive additionally contains a stabilizing amount of a saccharide.

10. The pharmaceutical composition of claim 9, wherein said saccharide is selected from the group consisting of dextrans, dextrans, polysaccharides, disaccharides and monosaccharides.

11. The pharmaceutical composition of claim 10, wherein said monosaccharide is selected from the group consisting of dextrose, fructose, D-glucose and L-glucose.

12. The pharmaceutical composition of claim 9, wherein said saccharide is a mixture of a substance selected from the group consisting of dextrans, dextrans and monosaccharides.

13. The pharmaceutical composition of claim 5, wherein said adhesive additionally contains a stabilizing amount of an organic weak proton donor.

14. The pharmaceutical composition of claim 13, wherein said organic weak proton donor is a carboxylic acid.

15. The pharmaceutical composition of claim 14 wherein said carboxylic acid is selected from the group consisting of citric acid, oxalic acid, ascorbic acid and benzoic acid.

16. The pharmaceutical composition of claim 13, wherein said composition is substantially anhydrous.

17. The pharmaceutical composition of claim 13 comprising, in weight percentages, about 0.5% to about

-19-

50% δ -aminolevulinic acid, and about 10% to about 95% of an adhesive.

18. A method of stabilizing δ -aminolevulinic acid or a pharmaceutical equivalent thereof, comprising mixing said δ -aminolevulinic acid or said pharmaceutical equivalent thereof with an anhydrous, flexible, finite pharmaceutically acceptable carrier suitable for topical administration.

19. The method of claim 18, wherein a weak organic proton donor is also added to the mixture.

20. The method of claim 19, wherein said weak organic proton donor is a carboxylic acid.

21. The method of claim 18, wherein said carrier is an adhesive.

22. The method of claim 21, wherein said adhesive is a pressure sensitive adhesive.

23. The method of claim 21, wherein said adhesive is selected from the group consisting of bioadhesives and polymeric adhesives.

24. The method of claim 23, wherein said polymeric adhesive is selected from the group consisting of an acrylic, a silicone-based adhesive, a vinyl acetate adhesive, and a natural or synthetic rubber-based adhesive, or mixtures thereof.

25. The use of δ -aminolevulinic acid or a pharmaceutical equivalent thereof for the preparation of a transdermal drug delivery device comprising a therapeutically effective amount of said δ -aminolevulinic acid or pharmaceutical equivalent thereof in a flexible

-20-

finite carrier for application to skin or other dermal
membrane of a mammal.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US95/10879

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/13.

US CL :514/671

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. : 514/671

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.
A,P	US, A, 5,369,142 (CULBERTSON ET AL.) 29 November 1994, column 4, lines 27 TO 45.	1-25

☐

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 document 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)	*A*	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

05 DECEMBER 1995

Date of mailing of the international search report

26 DEC 1995

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

THEODORE J. CRIARES

Telephone No. (703) 308-1235

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR
FOR PHOTODYNAMIC
THERAPY AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: MARLEN, TAMMIE K
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

CONCISE EXPLANATION OF RELEVANCE

Documents J3-J28 and J30-J37 listed on the attached PTO/SB/08 are exhibit documents of a Petition for Inter Partes Review. A copy of the Petition for Inter Partes Review, dated October 19, 2021 is submitted herewith (document J29). Exhibit US 2009/0324727 A1 was previously cited in an Information Disclosure Statement filed November 12, 2020.

Document J1 is an unpublished co-pending application filed September 28, 2021.

Document J2 is an unpublished co-pending application filed October 21, 2021.

FEE

Fees in the amount of \$260.00 to cover the fee associated with an information disclosure statement are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required for this application to Deposit Account Number 19-0741.

Respectfully submitted,

Date November 18, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

Electronic Patent Application Fee Transmittal

Application Number:	16791004			
Filing Date:	14-Feb-2020			
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS			
First Named Inventor/Applicant Name:	Thomas Boyajian			
Filer:	Glenn Law/Effie Hale			
Attorney Docket Number:	067286-0410			
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	260	260
Total in USD (\$)				260

Electronic Acknowledgement Receipt

EFS ID:	44320106
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	18-NOV-2021
Filing Date:	14-FEB-2020
Time Stamp:	16:39:22
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$260
RAM confirmation Number	E2021AHG40153004
Deposit Account	190741
Authorized User	Effie Hale

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

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	067286-0410_IDS_SB08.pdf	124941	no	3
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Warnings:					
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This is not an USPTO supplied IDS fillable form					
2	Foreign Reference	PCTWO96_06602.pdf	2237829	no	23
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3	Non Patent Literature	AffidavitDuncanHall.pdf	7668989	no	90
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4	Non Patent Literature	AGOSTINISetal.pdf	2771418	no	32
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5	Non Patent Literature	AktiliteManual_Metvixia.pdf	2640689	no	40
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6	Non Patent Literature	AmeluzPrescribingInfo.pdf	941814	no	12
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7	Non Patent Literature	BERARDESCAetal.pdf	5224659	no	4
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9	Non Patent Literature	BluU_OperatingManual.pdf	954080	no	17
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30	Non Patent Literature	SAKAMOTOetal.pdf	3583126	no	18
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Information:					
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Warnings:					
Information:					

35	Non Patent Literature	WILLEY_PubmedListing.pdf	786837 062f846652059ca90cdd20c44bacb0572927bc7e	no	6
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Information:					
36	Non Patent Literature	WOLFetal.pdf	5166899 aa083360ebdcdb43dd42c4e371e0c34640b9c6c	no	5
Warnings:					
Information:					
37	Transmittal Letter	067286-0410_IDSTrans.pdf	119001 7190ed74268bdc4baef00d44144635cf1548e609	no	2
Warnings:					
Information:					
38	Fee Worksheet (SB06)	fee-info.pdf	38154 7116b043391b5b80786632bbba5fa9912666e11a	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			85593158		
<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>					

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: December 20, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			
	K1	11,135,293-B2	10-05-2021	LUNDAHL ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				

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 ⁶
	K2	Australian Examination Report, Application No. 2020267186, 11/19/2021, 6 pages	
	K3	USPTO Office Action, 17/487,698 (067286-0437), 12/17/2021, 21 pages	
	K4	Zhang et al., "Topical 5-Aminolevulinic Photodynamic Therapy with Red Light vs Intense Pulsed Light for the Treatment of Acne Vulgaris _ A Split Face, Randomized, Prospective Study," DERMATO-ENDOCRINOLOGY, 2018, VOL. 9, NO. 1, e1375634 (9 pages)	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

Electronic Acknowledgement Receipt

EFS ID:	44565752
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	20-DEC-2021
Filing Date:	14-FEB-2020
Time Stamp:	16:37:20
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	Transmittal Letter	067286-0410_IDSTransmittal.pdf	119985 d5237287e8c76101510dec572a0da303816ec46e	no	3

Warnings:

Information:					
2	Non Patent Literature	AU_OA.pdf	1818629	no	6
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Warnings:					
Information:					
3	Non Patent Literature	OA_0437_121721.pdf	2194507	no	21
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Warnings:					
Information:					
4	Non Patent Literature	ZHANG.pdf	1419569	no	9
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5	Information Disclosure Statement (IDS) Form (SB08)	067286-0410_IDS_SB08.pdf	108024	no	1
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
Total Files Size (in bytes):			5660714		
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: MARLEN, TAMMIE K
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

CONCISE EXPLANATION OF RELEVANCE

Documents K1 and K4 listed on the attached Form PTO/SB/08 are documents cited in a PTO Office Action of a co-pending case (serial no. 17/487,698). The relevance of the references can be found in the PTO Office Action of the co-pending case. A copy of the PTO Office Action in the co-pending case is being submitted herewith (document K3). The cited documents are in English.

The US application number of document K1, 17/109,311, was previously cited in an Information Disclosure Statement filed January 4, 2021.

Document K2 listed on the attached PTO/SB/08 is a copy of an Examination Report issued in an Australian application dated November 19, 2021.

STATEMENT UNDER 37 CFR §1.97(e)

For document K2, the undersigned hereby states in accordance with 37 CFR §1.97(e)(1) that each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three (3) months prior to filing of this Statement.

STATEMENT UNDER 37 CFR §1.97(e)

For documents K1, K3 and K4, the undersigned hereby states in accordance with 37 CFR §1.97(e)(2) that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of the information disclosure statement.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date December 20, 2021

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371



UNITED STATES PATENT AND TRADEMARK OFFICE

USPTO Automated Interview Request (AIR)

Jan 17 2022

This paper requesting to schedule and/or conduct an interview is appropriate because:

This submission is requested to be accepted as an authorization for this interview to communicate via the internet. Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned concerning scheduling of the interview via video conference, instant messaging, or electronic mail, and to conduct the interview in accordance with office practice including video conferencing.

Name(s) :

Kiri Lee Sharon

S-signature:

/Kiri Lee Sharon/

Registration Number:

71828

U.S. Application Number:

16791004

Confirmation Number:

2631

E-mail Address:

ksharon@foley.com

Phone Number:

+1 2022954092

Proposed Time of Interview:

1-24-2022 11:00 AM ET

Alternative Proposed Time(s) of Interview:

1-24-2022 1:00 PM ET

Preferred Interview Type:

Telephonic

I am the applicant or applicant's representative for this application.

Topic for Discussion:

Proposed agenda to be provided



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16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
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FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			01/27/2022	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):

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<i>Applicant-Initiated Interview Summary</i>	Application No. 16/791,004	Applicant(s) Boyajian et al.		
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
TAMMIE K MARLEN	Primary Examiner	Telephonic
Kiri Lee Sharon	Attorney of Record	
Glenn Law	Attorney of Record	

Date of Interview: 24 January 2022

Issues Discussed:

Proposed Amendment(s)

Prior to the interview, the Applicant's representative submitted the attached proposed amendments. The Examiner indicated that the amendments would overcome the previous rejections under 35 USC 112, 102, and 103, however such amendments would likely necessitate new rejections under 35 USC 112(b). The Examiner and Applicant's representatives discussed ways to overcome this possible rejection, including claiming the light uniformity shown in Figure 8 of the application. No agreement was reached about specific language and the Examiner indicated to Applicant's representatives that in the next response, it would be beneficial to clearly explain where there is support and explanation for the claim amendments.

☒ Attachment

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
<p>Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04</p> <p>Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing</p>	

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AGENDA

A. Discuss the following proposed amendments.

1. (Currently Amended) A system for photodynamically diagnosing or treating a patient, comprising:

an illuminator comprising at least five panels connected by nested hinges on inner side surfaces of adjacent panels, the nested hinges being configured so as to allow illumination between the at least five panels to reduce optical dead space,

light sources disposed on surfaces of the at least five panels ~~a surface of the illuminator~~, the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources,

one of the at least five panels positioned as a center panel configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel,

wherein each of the at least five panels has two long edges and two short edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the short edges compared to the intensity of light emitted not proximate the short edges.

2. (Original) The system of claim 1, wherein the illuminator is configured to uniformly illuminate the treatment surface when the treatment surface is at a distance of two to four inches from the illuminator.

3. (Original) The system of claim 1, wherein the illuminator is configured to output red light at an intensity of about 30 J/cm² to about 150 J/cm².

4. (Original) The system of claim 1, wherein the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm².

5. (Original) The system of claim 1, wherein a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm.

6. (Currently Amended) A method of photodynamically diagnosing or treating a patient, comprising:

positioning an illuminator proximate to the patient, the illuminator comprising at least five panels connected by nested hinges on inner side surfaces of adjacent panels, the nested hinges being configured so as to allow illumination between the at least five panels to reduce optical dead space; and

uniformly illuminating a treatment surface of the patient with light sources disposed on the at least five panels of the illuminator,

wherein each of the at least five panels has two long edges and two short edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the short edges compared to the intensity of light emitted not proximate the short edges.

7. (Original) The method of claim 6, wherein the nested hinges are mounted to inner side surfaces of adjacent panels.

8.-10. (Cancelled).

11. (Original) The method of claim 6, further comprising determining a size of the treatment surface of the patient using a sensor.

12. (Original) The method of claim 6, further comprising determining a shape of the treatment surface of the patient using a sensor.

13. (Original) The method of claim 6, wherein at least one panel includes tabs outwardly extending from a top side and a bottom side, the tabs being configured to receive an adjacent panel therein.

14. (Original) The method of claim 11, further comprising adjusting an overall light dose with a controller based on the determined size of the treatment surface.

15. (Original) The method of claim 12, further comprising adjusting an overall light dose with a controller based on the determined shape of the treatment surface.

16. (Original) The method of claim 11, further comprising adjusting positioning of panels with at least one actuator based on the determined size of the treatment surface.

17. (Original) The method of claim 12, further comprising adjusting positioning of panels with at least one actuator based on the determined shape of the treatment surface.

18. (Currently Amended) The method of claim 6, further comprising changing intensities of the light sources of the illuminator with a controller in accordance with information received from at least one sensor relating to a curvature of the treatment surface.

19. (Currently Amended) The method of claim 6, wherein at least one panel includes a recess configured to receive a flange of [[a]] one of the nested hinges ~~hinge~~.

20. (Original) The method of claim 6,
wherein the illuminator comprises at least three first panels having first widths, at least two second panels having second widths, wherein each of the second widths of the at least two second panels is narrower than each of the first widths of the at least three first panels; and
wherein the at least three first panels and the at least two second panels are connected in an alternative manner such that each of the at least two second panels has a first lateral side connected to a respective one of the at least three first panels and a second lateral side connected to another respective one of the at least three first panels.

21. (New) The system of claim 1, further comprising a joint for one of the nested hinges, the joint positioned substantially flush with an outer front surface of one panel of the at least five panels.

22. (New) The method of claim 19, wherein the recess is positioned at an inner side surface of the at least one panel.

B. Discuss the claim rejections under 35 U.S.C. § 112

Claims 1-20 were rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph. The proposed amendments are believed to address the § 112(b) rejections.

C. Discuss the claim rejections under 35 U.S.C. § 102

Claims 1, 2, 6, 7, 13, 18, and 19 were rejected under 35 U.S.C. § 102(a)(1) over U.S. Patent Publication No. 2007/0283655 (“Tobin”). Claims 1, 2, 5-7, and 18 were rejected under 35 U.S.C. § 102(a)(1) over U.S. Patent Publication No. 2005/0075703 (“Larsen”).

Tobin discloses an illuminator including panels of different sizes (*see* Fig. 2). Tobin does not disclose a system or method “wherein each of the at least five panels has two long edges and two short edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the short edges compared to the intensity of light emitted not proximate the short edges.” Larsen discloses an illuminator with light sources in the form of tubes (*see* Fig. 17b). Larsen does not disclose or teach such features.

D. Discuss the claim rejections under 35 U.S.C. § 103

Claims 3-5 were rejected under 35 U.S.C. § 103 over Tobin in view of U.S. Patent Publication No. 2003/0216795 (“Harth”). Claims 11, 12 and 14-17 were rejected under 35 U.S.C. § 103 over Tobin in view of U.S. Patent Publication No. 2013/0066404 (“Tapper”). Claims 3 and 4 were rejected under 35 U.S.C. § 103 over Larsen in view of Harth. Claims 11, 12, and 14-17 were rejected under 35 U.S.C. § 103 over Larsen in view of Tapper. Claim 20 was rejected under 35 U.S.C. § 103 over Larsen.

Neither Harth nor Tapper discloses or teaches a system or method including the noted features.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 10, 2022 <i>(use as many sheets as necessary)</i>				Complete if Known	
Sheet 1 of 1		Application Number		16/791,004	
		Filing Date		2/14/2020	
		First Named Inventor		Thomas BOYAJIAN	
		Art Unit		3792	
		Examiner Name		MARLEN, TAMMIE K	
		Attorney Docket Number		067286-0410	

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)			
	K1	2010/0174222-A1	07-08-2010	MCDANIEL, DAVID H.	
	K2	2015/0290470-A1	10-15-2015	TAPPER ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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	K3	WO-2013/110021-A1	07-25-2013	HARVARD BIOSCIENCE INC , UNIV NEW YORK STATE RES FOUND		

NON PATENT LITERATURE DOCUMENTS			
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	K4	Japanese Office Action and English translation, Application No. 2019-555822, 1/11/2022, 13 pages	T
	K5	USPTO Office Action, 16/808,631 (067286-0409), 1/21/2022, 28 pages	

Examiner Signature		Date Considered	
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PATENT TERM ADJUSTMENT STATEMENT UNDER 37 CFR 1.704(d)

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3792
Examiner Name	MARLEN, TAMMIE K
Practitioner Docket No.	067286-0410

APPLICANT HEREBY STATES THE FOLLOWING (please review 37 CFR 1.704(d) before filing this form):

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Signature	/Glenn Law/	Date	02-10-2022
Typed or Printed Name	Glenn Law	Practitioner Registration Number	34,371
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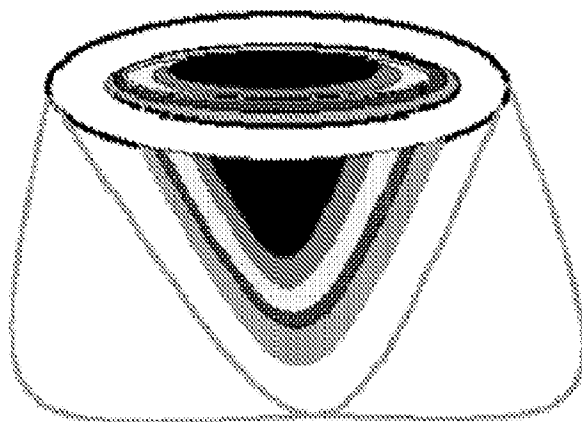
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[Continued on nextpage]

(54) Title: METHOD FOR EVALUATING TISSUE INJURIES

FIG 4C



(57) Abstract: Aspects of the invention relate to meth-
ods and devices for evaluating tissue injuries. In some
embodiments, the invention provides methods and
devices for evaluating tissue injuries based on infrared
emission spectra and/or emission levels from injured
tissue. In some embodiments, the invention provides
methods and devices for evaluating skin injuries (e.g.,
skin burns) and for targeting treatment delivery to in-
juries including skin injuries.

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-1-

METHODS FOR EVALUATING TISSUE INJURIES

RELATED APPLICATIONS

This application claims priority under 35 U.S.C. § 119(e) from U.S. Provisional Application Serial No. 61/589,292 having a filing date of January 20, 2012 and entitled "METHODS FOR EVALUATING TISSUE INJURIES," from U.S. Provisional Application Serial No. 61/637,266 having a filing date of April 23, 2012 and entitled "METHODS FOR EVALUATING TISSUE INJURIES," and from U.S. Provisional Application Serial No. 61/638,481 having a filing date of April 25, 2012 and entitled "METHODS FOR EVALUATING TISSUE INJURIES," the contents of each of which are incorporated herein in their entirety by reference.

BACKGROUND

A burn is a type of injury to skin or another tissue that can be caused by a variety of different insults, including, for example, heat, electricity, chemicals, light, radiation or friction. It is often important to determine the extent of a burn injury because, depending on its severity, a burn may be treated with first aid without the need for hospitalization or professional medical care or may require more specialized treatment such as those available at specialized burn centers. Furthermore, managing burn injuries properly is important because they are common, painful and can result in disfiguring and disabling scarring, amputation of affected parts or death in severe cases. The treatment of burns may include the removal of dead tissue (debridement), applying dressings to the wound, fluid resuscitation, administering antibiotics, and skin grafting, depending on the depth and severity of the burn.

Similarly, appropriate treatments for other injuries or wounds (including trauma injuries, contusions, cuts, abrasions, etc.) depend on the extent and severity of the injured or wounded tissue. However, it is often difficult to assess the extent or severity of a tissue injury immediately after the injury occurs. It can take several days for the full extent of an injury to become apparent through visible physical changes of the injured tissue. This delay can make it difficult to select the most appropriate treatment soon after the injury occurs.

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SUMMARY OF THE INVENTION

In some embodiments, aspects of the invention relate to methods and devices for evaluating tissue injuries by analyzing emission spectra and/or emission levels from injured tissue. In some embodiments, infrared emissions from a tissue region can be used to evaluate the presence and/or extent of an injury in the tissue region. According to aspects of the invention, the level of infrared (IR) emission from a tissue is affected by physical changes in the tissue that can be caused by injury. In some embodiments, an injury is a burn. In some embodiments, an injury is a traumatic injury. In some embodiments, an injury is a cut, a tear, an abrasion, or other physical disruption of tissue integrity, for example due to chemical exposure, radiation, friction, and/or natural disease changes. In some embodiments, an injury can result from a pressure wave (e.g., from an explosion or other source of pressure blast).

In some embodiments, emissions (e.g., IR emissions) from an injured tissue can be used to determine the extent or severity of an injury soon after the injury occurs (e.g., within several minutes to several hours of the injury), and long before the full extent or severity of the injury can be determined from visible tissue changes. In some embodiments, relative emission intensities (e.g., relative IR emission intensities) from different areas of an injured tissue can be used to identify different levels of injury severity within the injured tissue. In some embodiments, the rate of change of emission intensity as a function of distance within an injured tissue can be used to determine different levels of injury within the tissue. It should be appreciated that emission intensities (e.g., relative emission intensities) can be analyzed using any suitable method. In some embodiments, emission levels are analyzed and/or displayed (e.g., using a color display), in some embodiments, changes in emission levels are analyzed and/or displayed. Methods described herein can be useful to identify areas of severe injury (e.g., deep burns, third degree burns, deep or severe blunt force injury, etc.), areas of minor injury (e.g., shallow burns, first degree burns, mild bruising or contusion, etc.), or areas of intermediate injury (e.g., second degree burn). In some embodiments, the areas of highest injuries within a tissue are identified as peaks or valleys of emission (e.g., highs or lows of IR emission). In some embodiments, the severity of the injury is evaluated by quantifying a peak or a valley (e.g., by calculating an area under the curve representing the peak or valley, for example by calculating the area under half the height of the peak or valley). However, it should be appreciated that any technique may be used to quantify different regions of emission intensity.

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In some embodiments, different levels of emission are determined using a detector (e.g., an IR detector, for example a far-IR detector) that can detect and/or display small differences in the amount of IR energy emitted from an object (e.g., small differences in IR emission intensity). In some embodiments, a detector can detect difference in IR emission intensities that correlate with a temperature difference of 1 °C, or less (e.g., 0.1 °C, 0.01 °C, or 0.001 °C). In some embodiments, a detector includes or is connected to a display that contains a palette (e.g., a color palette, a greyscale palette, an intensity palette, a heat map, or any combination thereof) that can distinguish IR emission intensities that correlate with a temperature difference of 1 °C, or less (e.g., 0.1 °C, 0.01 °C, or 0.001 °C). In some embodiments, a detector includes a display (e.g., a high resolution display) that contains a palette (e.g., color or greyscale or a heat map or other palette) encompassing a temperature range of 0 °C to 50 °C, 10 °C to 50 °C, 10 °C to 40 °C, 15 °C to 40 °C or 18 °C to 37 °C.

In some embodiments, patterns of IR emission levels from an injured tissue (e.g., a wounded tissue or a burned tissue, for example burned skin) can be used to rapidly evaluate the severity of the wound or burn (and/or patterns of burn severity) soon after the injury occurs. This is much sooner than is currently possible. This allows for an appropriate treatment to be implemented much sooner, without needing to wait for visual signs of wound or burn severity to develop. This means that treatment can be more effective. It should be appreciated that injuries such as burns (but also other wounds, for example resulting from blunt force trauma) are often complex. An injury (e.g., a burn) can produce a range of tissue injury from regions of severe injury to regions of mild injury. An injury (e.g., a skin injury) often includes a complex pattern of regions of severe injury (e.g., deep tissue burns) surrounded by regions of lesser injury (e.g., mild burns or superficial burns). It is often difficult to determine visually which areas of an injury are more severely affected than others for several days (during which the injured tissue progressively dies and/or heals). However, methods described herein can be used to identify a pattern of tissue injury (e.g., identifying skin areas having different levels of wound or burn severity within a region of injured skin). Accordingly, methods described herein can be used to map an injury to identify portions that are more severely injured than others and that will require more intense treatment than others. In some embodiments, specific levels of IR emission in one or more regions of a wound or burn (e.g., detected as temperature levels, or other measures of the amount of IR energy coming from the injury, for example measured as energy per unit area, or other measures of IR emission) can be used to determine the severity of the wound or burn or

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region thereof (for example with regions of greater injury having lower surface temperature than region of lower injury in some cases). However, in some embodiments, the depth of a wound or burn can be assessed by determining the rate of change of IR emission levels across a wound or burn. In some embodiments, steep changes as a function of distance are indicative of shallow wounds or burns whereas shallow changes as a function of distance are indicative of deeper wounds or burns. In some embodiments, a point or area of low IR emission can be used to identify a center of a region of burned tissue being evaluated. In some embodiments, the point or area of a burn that has the lowest level of IR emission can be identified as the point or area that is the "coldest" in an infrared image of the burned tissue. In some embodiments, this represents the region that is the most burnt or damaged. It should be appreciated that the center of a burn can be approximately the geometrical center of a burned region of tissue (e.g., skin). However, in many instances burns do not have regular or symmetrical geometric shapes. For example, burns caused by fires or chemical exposure can have complex shapes and patterns. Nonetheless, a region of low IR emission (e.g., the region of the burned tissue having the lowest levels of IR emission, or a local minimum of infrared emission surrounded by areas having higher levels of IR emission) can be used as a point of origin for an analysis to determine the severity of the burn (e.g., the depth of the burn). In some embodiments, the region of lowest IR emission (or one or more local minima of IR emissions) can be used as a reference point to evaluate the amount of change in IR emission levels as a function of the distance from the reference point(s). In some embodiments, a gradual change in IR emission levels from a point of low emission is indicative of a deep burn, whereas a rapid change in IR emission levels as a function of distance from a point of low emission is indicative of a shallow burn. Accordingly, the slope of change in IR emission levels as a function of distance from a point of low IR emission can be used to evaluate the severity and/or depth of a burn or of a region of a burn surrounding a local low point. It should be appreciated that reference rates of change (e.g., slopes of IR emission curves as a function of distance from a point of low IR emission) can be determined for different burn severities (burn depth, degree of burn, etc.). It also should be appreciated that reference rates for different burn severities can be determined for different types of tissue (e.g., skin), for different types of injury (e.g., fire, chemical exposure, radiation, etc.), for different ages of individual (e.g., child, teen, young adult, middle-aged, 0-10 year olds, 10-20 year olds, 20-30 year olds, 30-40 year olds, 40-50 year olds, 50-60 year olds, 60-70 year olds, 70-80 year olds, 80-90 year olds, etc.), different subjects (humans, non-human mammals, birds,

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reptiles, etc.), different disease conditions, and for other parameters. These reference rates of change can be used to evaluate a rate of change in a tissue being evaluated (e.g., at the time of or soon after an injury). However, in some embodiments, different relative rates of change in IR emission levels as a function of distance across one or more burned regions can be used to determine the relative severity of the different burned regions in a subject without needing to compare them to one or more external (or predetermined) references. In some embodiments, both external and internal rates of change can be used to evaluate the burn severity of a subject (e.g., a burn patient). In some embodiments, the value of the difference between the highest level of IR emission intensity and lowest level of IR emission intensity within the injured tissue, or the number of different levels of IR emission intensity that can be detected, or the value of the difference between the highest or lowest level of IR emission intensity and a reference level of IR emission intensity corresponding to unburnt skin, or any other measure of IR emission levels, or any combination thereof, may be used to evaluate the extent or severity of a burn.

Accordingly, patterns of burn severity can be identified for the subject based on patterns of IR emission levels and these can be used to provide an early patient prognosis and/or an early treatment recommendation (e.g., within one or a few hours of the injury). In some embodiments, methods described herein are used to determine the size and shape of burnt tissue. In some embodiments, methods described herein are used to identify the most severely burnt regions within a burnt tissue.

It should be appreciated that other tissue injuries (e.g., wounds) can be evaluated using similar techniques, including for example obtaining and analyzing IR emissions from an injured tissue and identifying one or more local maxima or minima (e.g., peaks or valleys) of IR emission. In some embodiments, the rate of change of IR emission across an injured tissue (e.g., from a reference point, e.g., a center, of a local peak or valley) is used to evaluate the severity of the injury. In some embodiments, the size of the range of IR emission intensities within the injured tissue (e.g., the value of the difference between the highest and lowest level of IR emission intensity, or the number of different levels of IR emission that can be detected, etc., or any combination thereof) is used to determine the severity of the injury at different positions in an injury (e.g., at different positions on injured skin of a subject). In some embodiments, the size of a local peak or valley of IR emission is used to determine the severity of the injury at that position. In some embodiments, IR levels or patterns are used to determine the size and shape of

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an injury. In some embodiments, IR levels or patterns are used to identify the most severely injured regions within an injured tissue.

In some embodiments, a method comprises identifying an IR maximum or minimum (e.g., a peak or a valley of IR radiation) in a tissue. In some embodiments, this peak or valley represents a region of maximal tissue damage (e.g., burn or other wound) within an area of injury. In some embodiments, the severity of the injury can be evaluated by determining the properties of the peak or valley (e.g., size, for example by evaluating the area under half the peak or valley height, or the slope of the IR changes surrounding the peak or valley) or by patterns or profiles of IR radiation surrounding the peaks or valleys. It should be appreciated that in some embodiments, the most injured tissue portion may be the portion with the highest IR emission (e.g., highest apparent temperature or "hottest"). However, in other embodiments, the most injured tissue portion may be the portion with the lowest IR emission (e.g., lowest apparent temperature or "coldest"). The IR emission from the most injured tissue will depend, at least in part, on the emissivity of the most injured tissue, in addition to factors such as the impact of the injury on the amount of blood flow under the injured region. In the case of a burn, the most severely burned area can be detected as the "coldest" area (the area with the lowest IR emission). Accordingly, in some embodiments a method comprises a) determining the center (or one or more regions of higher damage) of a complex burn by identifying the regions that have the lowest levels of infrared emission (e.g., are the coldest), b) determining regions of healthy tissue surrounding the burn, or regions of lowest burn (healthiest burn regions) by identifying regions that have the highest levels of infrared emission (e.g., the warmest regions surrounding a burned tissue), and c) determining curves of infrared emission change (e.g., curves temperature change), wherein the properties of the curves are indicative of the burn severity (for example, steep curves are indicative of less damage or shallow burns, flat curves are indicative of severe damage or deep burns). In some embodiments, there can be rings of high IR emission surrounding a center of a burn. In this case, a region of healthy tissue (e.g., as described in b) above) can be identified as a region of tissue or skin that has a consistent IR emission that is similar to other tissue or skin that is known to be healthy, for example, uninjured tissue or skin on the body of the injured subject. This level may be lower than a ring of high IR emission immediately surrounding a burn.

In some embodiments, an analysis of IR profiles or patterns can be performed as a vector analysis wherein the vectors radiate from the areas of most damage and their properties are

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indicative of the degree of burn at any particular location within the burn. However, any suitable analytical technique (e.g., mathematical analysis, computer-based analysis, calculation, geometric comparison, or other assessment or evaluation) can be used to determine one or more levels of burn severity (or other wound severity) as a function of detected patterns of IR emission levels over the surface of a burn (or a portion of a burn, or a portion of skin suspected of being burned or otherwise injured). In some embodiments, an analysis can be automated (for example with one or more analytical steps performed using a processor on a computer).

In some embodiments, patterns of burn severity based on IR emission patterns can be evaluated immediately after an injury or as soon as a few hours after a burn. In some embodiments, the patterns of emissivity from a burn are more distinct within the first few hours after a burn than a few days later. Accordingly, in some embodiments a wound or burn can be evaluated by determining a pattern of IR emissions from the wounded or burnt tissue within a few hours (e.g., 1-3, 3-6, 6-12, 12-18, 18-24 hours) of tissue injury. For example, in some embodiments, a wound or burn can be evaluated by determining a pattern of IR emissions from the wounded or burnt tissue within 1 hour of tissue injury (e.g., immediately after the injury, or 1-5 minutes, or about 5 minutes, 5-15 minutes, 15-30 minutes, about 30 minutes, 30-45 minutes, 45-60 minutes, or about 1 hour after tissue injury). In some embodiments, a wound or burn can be assessed by, for example, analyzing the slope of change in levels of emissivity along one or more directions in at least part of the wound or burn (e.g., in one or more directions radiating out from a region of low or high IR emission). In some embodiments, vectors representing the rate of change of IR emissivity can be determined. In some embodiments, vectors originating in an area of high wound or burn are determined. In some embodiments, an area of high burn is identified as an area of low emission (e.g., an area that is shown as cold using an IR detection device that is calibrated for and/or provides a temperature readout). In some embodiments, the location of the most burnt tissue is identified as the region with the lowest emission levels (e.g., showing up as the coldest using an IR detection device that is calibrated for and/or provides a temperature readout.). It should be appreciated that any suitable infrared detection device can be used. In some embodiments, an infrared camera can be used. In some embodiments, an infrared detection device is calibrated to detect different temperatures. However, in some embodiments, an infrared detection device is calibrated to be sensitive to different levels of IR emissivity that can be affected by surface properties independent of temperature. Accordingly, an infrared detection device can be calibrated to detect contrasts between different surface properties (e.g.,

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whether they are shiny or not, or other surface properties) that can be detected even if they have the same temperature. Accordingly, an infrared camera (e.g., a forward looking IR camera or detector) or other infrared detection device can be calibrated to be sensitive to surface contrasts between different tissue regions (e.g., calibrated or limited to detect particular IR ranges, for example far IR or subsets of wavelength ranges within the far IR). In some embodiments, a detector device include two or more detectors, for example each for a different type of IR (e.g., two or three of near, mid, or far IR). In some embodiments, a detector device includes a single detector that can detect two or more types of IR (e.g., two or three of near, mid, or far IR).

It should be appreciated that different IR spectra can be evaluated. In some embodiments, near IR is evaluated. In some embodiments, mid-IR is evaluated. In some embodiments, far IR is evaluated. In some embodiments, two or more are evaluated. In some embodiments, IR patterns are evaluated and or overlaid with other information (e.g., visible or UV patterns or images). In some embodiments, mid-IR data can be detected by using a suitable detector and a suitable excitation energy. If two or more detectors are used, they can be aligned to allow the images or data to be overlaid.

It should be appreciated that a rapid and correct assessment of a tissue burn can be clinically important. As a general clinical rule, an adult with burns on more than 20% of the body surface area, or a child with burns on more than 10% of the body surface area, will require intravenous fluid replacement. However an intravenous line may be necessary to achieve adequate analgesia for a much smaller burn, and in some instances (e.g., for some children) fluid replacement may be required because of vomiting. It also should be appreciated that a patient's (e.g., a human patient's) prognosis can be evaluated based upon the percentage of the patient's body surface area that is burned. In some embodiments, as a rough guide, if the age of the patient and percentage of body burned are added together, a score of 100 or above is indicative that the burn is likely to be fatal. For example, a child can survive a relatively large burn, but a smaller burn is potentially fatal for an elderly patient.

Similarly, for other injuries, an early assessment of an injury can be helpful to initiate an appropriate and/or targeted treatment as soon as possible.

In some embodiments, IR imaging as described herein also can be used to evaluate or detect other conditions such as diseases (e.g., skin lesions, cancerous or pre-cancerous lesions, acne, rashes, psoriasis, other inflammatory conditions, or other skin conditions). As described herein, an IR pattern or profile can be used to evaluate and or determine the extent and or

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severity of a condition (e.g., a skin condition). In some embodiments, a method involves comparing IR patterns or profiles to reference patterns or profiles associated with a condition of interest. In some embodiments, an IR pattern can be used as the basis of a targeted treatment. For example, treatment can be targeted to those areas that are identified as being the most severely affected. In some embodiments, a bandage (e.g., bandaid or other medically suitable support material, for example with or without an adhesive strip for application to a tissue surface such as a skin surface) can be prepared with a spatial pattern of treatment (e.g., of one or more antibiotics, anti-inflammatory compounds, or other treatment materials) that corresponds to one or more features of the IR pattern. In some embodiments, a bandage is a therapeutic bandaid. In some embodiments, a bandage is a preparative bandaid. For example, it can contain a pattern of debriding compositions to prepare a burned or otherwise injured tissue for subsequent treatment. In some embodiments, a bandage may contain both preparative and treatment compositions. In some embodiments, a bandage can be printed with an appropriate pattern of one or more compositions. However, compositions can be deposited on a bandage in an appropriate pattern using any suitable technique. It should be appreciated that a bandage can be of any suitable size to cover an area of injured (e.g., burned or wounded) tissue. In some embodiments, two or more bandages may be used to cover an injured tissue area or a portion thereof.

It should be appreciated that infrared contrast imaging as described herein can be used to evaluate different aspects of biological tissues, and also can be used to evaluate other materials (for example metals, wood, plastic, etc., for example to detect damage or other physical modifications).

These and other aspects are described in more detail below and with reference to the drawings.

DESCRIPTION OF THE DRAWINGS

FIG. 1A illustrates a technique for obtaining IR data for different types of burns;

FIG. 1B illustrates Jackson's Burn Model showing distinct areas of tissue damage within a burn;

FIG. 1C shows infrared (IR) emission from a burn and illustrates how a burn can be assessed using IR-based techniques described herein;

FIG. 2A illustrates a burn model using pig skin showing surface squares of tissue regions that are targeted for burning, different squares can be exposed to different temperatures and/or for different times to model different levels of burn severity ;

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FIGs. 2B and 2C illustrate IR spectra from burned tissue regions within the first day after a burn injury;

FIG. 2D illustrates a non-limiting technique for analyzing IR data;

FIG. 3A illustrates a burn model;

FIG. 3B shows levels of IR emissions across 3 different burned regions;

FIG. 3C illustrates deep burn patterns (green and blue) and shallow burn patterns (red);

FIG. 4A shows IR emission patterns from non-limiting examples of burned tissue;

FIG. 4B illustrates a model of a deep burn;

FIG. 4C illustrates a model of a shallow burn;

FIG. 5 shows a non-limiting example with several (7) distinguishable layers of tissue disruption one day after a burn;

FIG. 6A shows the IR patterns from top views of different burns;

FIGs. 6B and 6C show depth profile models;

FIGs. 7A-7B show the data and models of FIGs. 6A-6C in more detail;

FIG. 8 shows different IR profiles corresponding to different lines across one or more burned tissue regions;

FIG. 9A shows IR patterns of scars at 28 days after injury;

FIG. 9B shows IR patterns of burned tissue at 24 hours after injury;

FIG. 9C illustrates IR patterns of burned tissue at 24 hours, 72 hours, and 7 days after injury;

FIG. 9D illustrates that IR data at 24 hours after injury correlates with wound contraction and scar depth 4 weeks after injury;

FIG. 9E illustrates that IR data at different times after injury correlates with scar depth 4 weeks after injury;

FIG. 10 shows IR patterns for scars at 672 hours after injury, lines 4 and 5 show minimal scarring, characteristic ring destruction patterns are still evident on scarred skin whereas minimally scarred tissue shows no ring destruction;

FIG. 11 shows a high definition IR image of a day old burn;

FIGs. 12A-B provide a model for real burns based on infrared contrast imaging (IRCI) data, illustrating a shallower pattern of IR changes radiating from the center of a deep burn than for a shallow burn;

FIGs. 13A-C provide an example of an analysis of a burned tissue model and illustrates how shallow and deep burns can be identified based on patterns of IR emission (and the extent of change in IR emission from the center of a burn);

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FIG. 14 illustrates vectors representing patterns of IR emission changes from the centers of burned regions that can be used to evaluate burn depth (and, for example, to distinguish shallow burns from deep burns);

FIG. 15 illustrates non-limiting examples of IR emission profiles (shown as temperature profiles) across the diameter of a burn;

FIG. 16 illustrates non-limiting examples of vectors radiating from the points of lowest emission for shallow and deep burns;

FIG. 17A illustrates further non-limiting examples of vectors radiating from the points of lowest emission for several shallow and deep burns;

FIG. 17B illustrates a non-limiting example of a profile obtained from an IR image containing an irregular burn pattern;

FIG. 18A illustrates an IR pattern of a skin condition;

FIG. 18B illustrates several bandages printed with preparation or treatment compositions deposited in a pattern corresponding to one or more features of the IR pattern of the skin condition; and

FIG. 18C illustrates a bandage of FIG. 18B applied to the skin condition of FIG. 18A.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS OF THE INVENTION

In some embodiments, aspects of the invention relate to methods and devices for evaluating tissue injuries by analyzing emission spectra and/or emission levels (e.g., near IR, mid IR, far IR, or a combination thereof) from injured tissue. In some embodiments, aspects of the invention relate to methods and devices for detecting or evaluating tissue conditions (e.g., diseases or disorders) by analyzing emission spectra and/or emission levels (e.g., near IR, mid IR, far IR, or a combination thereof) from a target tissue (e.g., skin) suspected of having a disease or disorder. In some embodiments, infrared emissions from a tissue region can be used to evaluate the presence and/or extent of an injury or condition of the tissue region. According to aspects of the invention, the level of infrared emission from a tissue is affected by physical changes in the tissue that can be caused by injury or condition. In some embodiments, an injury is a burn. In some embodiments, an injury is a traumatic injury. In some embodiments, an injury is a cut, a tear, an abrasion, or other physical disruption of tissue integrity. In some embodiments, an injury can result from a pressure wave (e.g., from an explosion or other source of pressure blast). In some embodiments, a tissue condition can be a skin disease or disorder (e.g., an infection, inflammation, psoriasis, acne, cancer, or other condition or disorder).

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As used herein, the term "level of infrared emission" or "infrared emission level" refers to an amount of infrared energy emitted from a volume or surface. . In some embodiments, a level of infrared emission is a mean power per unit area (intensity) of radiation emitted from a volume or surface (e.g., a tissue or skin surface) across a particular band of wavelengths in the infrared range. In some embodiments, a level of infrared emission is a time averaged intensity of radiation emitted from a volume or surface (e.g., a tissue or skin surface) across a particular band of wavelengths in the infrared range. In some embodiments, a level of infrared emission is a maximum intensity of radiation emitted from a volume or surface (e.g., a tissue or skin surface) across a particular band of wavelengths in the infrared range over a period of time. In some embodiments, a level of infrared emission is a root mean square of intensity of radiation emitted from a volume or surface (e.g., a tissue or skin surface) across a particular band of wavelengths in the infrared range over a period of time.

In some embodiments, a level of infrared radiation is determined that comprises power per unit area (intensity) of radiation emitted, transmitted or reflected from a volume or surface (e.g., a tissue or skin surface) across a particular band of wavelengths in the infrared range. In some embodiments, levels of infrared radiation reflect relative intensities of infrared radiation emitted, transmitted, and/or reflected from across a volume or surface.

In some embodiments, infrared radiation from an injured tissue or object primarily comprises emitted infrared radiation and there is very little transmitted or reflected infrared radiation. In some embodiments, reflected infrared radiation may be reduced by using a filter or polarizing screen above or around an injured area to prevent external infrared radiation from reaching the tissue.

In some embodiments, levels of infrared radiation are determined using an infrared detection system (e.g., spectroscopy, thermography) to measure infrared radiation emitted (as opposed to being transmitted or reflected) from a volume or surface. However, in some embodiments, levels of infrared radiation are determined using infrared detection system (e.g., spectroscopy, thermography) to measure infrared radiation emitted, transmitted and/or reflected from a volume or surface.

In some embodiments, infrared radiation can be used to determine the temperature of objects where the emissivity of the surface is known or estimated. In some embodiments, levels of infrared radiation are displayed or reported as temperatures, but the differences in apparent temperature can be indicative of differences in emissivity (e.g., caused by a tissue injury or

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disorder) in addition to or instead of actual differences in temperature (e.g., due to inflammation or differences in blood flow through an injured tissue). It has been appreciated, as described herein, that tissue changes caused by an injury such as a burn can change the level and/or pattern of IR radiation that is emitted from the injured tissue, and that the degree of injury affects the amount of IR radiation that is emitted. The change in the amount of IR radiation that is emitted is affected in part by immediate changes to the tissue upon injury that alter the emissivity of the tissue (e.g., changes in density, surface texture, water content, etc., that are impacted by the injury). Accordingly, the amount of IR radiation that is emitted from an injured tissue (e.g., wounded or burned skin) can be used to evaluate the severity of the injury soon after the time of injury (e.g., within minutes to hours of the injury) as opposed to waiting for visual signs of injury to develop through natural physiological healing processes (that can take several days). This allows for appropriate medical treatment to be applied early after injury and also for the treatment to be appropriately targeted (e.g., to areas of most severe injury). Similarly, the extent and or severity of a disease or disorder that affects skin or tissue properties can be detected and/or evaluated using an IR analysis as described herein.

In some embodiments, the amount of IR radiation that is emitted from an injured tissue is measured using a device (e.g., a camera) that provides (e.g., displays) apparent temperatures of the tissue. However, other devices and techniques for detecting, measuring, or displaying the amount of IR radiation also can be used as aspects of the invention are not limited in this respect. In some embodiments, absolute levels of radiation do not need to be calculated, determined, and/or displayed, because differences in tissue injury severity or tissue condition can be determined based only on relative amounts of IR radiation for different portions of the tissue (e.g., of the injured tissue).

In some embodiments, an infrared camera or other infrared detection device can be used to detect or measure infrared emission levels from a target tissue of interest (e.g., from the surface, e.g., skin, of a tissue region that is injured or suspected to be injured and/or including surrounding tissue) of a subject. In some embodiments, far infrared emission levels are detected. However, in some embodiments, near or mid-infrared emission levels are detected, as aspects of the invention are not limited in this respect. In some embodiments, data obtained from an infrared detection device (e.g., an infrared camera) can be analyzed on a computer to detect patterns and/or levels of infrared emissions associated with the presence and/or extent of injury. These levels can be displayed (e.g., on a screen of the computer) using any suitable

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scheme (e.g., different colors, different identifiers for different zones, or any other suitable scheme, or any combination thereof). In some embodiments, the infrared emission information can be analyzed using a processor that is incorporated in the infrared detection device and the detected levels of infrared emission and/or the correlated levels of tissue injury can be displayed directly on the infrared detection device (e.g., camera). For example, different levels of hematomas, different degrees of burn, different burn depths, or other different levels of tissue damage can be displayed (e.g., on a screen) on the detection device. In some embodiments, the infrared detection device can be a hand-held camera (e.g., a forward looking infrared camera). However, immobilized detection devices (e.g., an immobilized camera, for example on a support such as a tripod) or larger detection devices also can be used as aspects of the invention are not limited in this respect. In some embodiments, a device can detect only one type of IR radiation (e.g., near, mid, or far). However, in some embodiments, a device can detect two or more types of IR radiation. In some embodiments, two or more different devices can be used. Information corresponding to different types of IR radiation can be overlaid and or combined with other information including for example visual or UV information.

In some embodiments, detection devices can be head-worn (WYSIWYG). In a non-limiting example of a head worn device, one or both eyes can see IR wavelengths, visible wavelengths, and or UV wavelengths. In some embodiments, both eyes can see one or more different wavelengths (or wavelength ranges) allowing for a stereoscopic display. In some embodiments, one or more images can be displayed as overlays to provide composite views of different types of data.

In some embodiments, aspects of the invention relate to using infrared patterns to evaluate tissue injuries (e.g., a wound or burn severity) or conditions based on the surface infrared emission levels (for example from skin) without requiring any dyes, labels, or energy input. In some embodiments, no irradiation is required since techniques described herein do not rely on reflected IR. For example, far IR data corresponding to thermal radiation can be obtained without using a dye or excitation energy. However, in some embodiments, one or more dyes or excitation energies can be used. For example, mid IR data can be obtained using an appropriate excitation energy in addition to a mid IR detector.

In some embodiments, the infrared emissions utilized with the methods and devices disclosed herein have a wavelength in the range of 0.7 μm to 25 μm or 8 μm to 25 μm . In some embodiments, the infrared emissions comprise emissions in the near infrared range, e.g.,

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emissions having a wavelength of about 0.7 μm to about 1.0 μm . In some embodiments, the infrared emissions comprise emissions in the short-wave infrared range, e.g., emissions having a wavelength of about 1 μm to about 3 μm . In some embodiments, the infrared emissions comprise emissions in the mid-wave infrared range, e.g., emissions having a wavelength of about 3 μm to about 5 μm . In some embodiments, the infrared emissions comprise emissions in the long-wave infrared range, e.g., emissions having a wavelength of about 8 μm to about 12 μm , or about 7 μm to about 14 μm . In some embodiments, the infrared emissions comprise emissions in the very-long wave infrared range, e.g., emissions having a wavelength of about 12 μm to about 30 μm . In some embodiments, the infrared emissions comprise emissions in the far infrared, e.g., emissions having a wavelength of about 15 μm to about 1000 μm .

The use of IR patterns to evaluate the severity of an injury (e.g., a skin wound or a skin burn) is illustrated by experimental models described with reference to some of the figures. However, it should be appreciated that these experiments are non-limiting and the techniques can be used to evaluate injuries (e.g., wounds or burns) in other contexts (e.g., for human tissue) or other conditions (e.g., skin diseases or disorders).

FIG. 1A illustrates a non-limiting method for obtaining IR data for different burns and correlating the data with different outcomes. Burns are created by contacting one end of heated metal bar (e.g., an aluminum bar) to the skin of a test animal (e.g., a pig). The metal bar can be heated using any suitable technique (e.g., by maintaining it in a water bath at a set temperature). Different temperatures and different contact times can be used to generate different levels of burn. For example, contact with a bar at 70 °C for 20 seconds can be used to create a superficial dermal burn, contact with a bar at 80 °C for 20 seconds can be used to create a mid-dermal burn, and contact with a bar at 80 °C for 30 seconds can be used to create a deep dermal burn. IR emissions from the burns can then be detected and/or measured using an appropriate IR detector. For example, the burns can be photographed using an IR camera (e.g., a forward looking infrared camera, for example, a FLIR T300 available from FLIR Systems, Inc.). The IR data (e.g., the thermal image obtained with the IR camera) can then be analyzed and compared with the outcomes of the burns (e.g., the wound contraction and/or the scar depth) at a later time (e.g., 4 weeks after the burn). It should be appreciated that burn outcomes can be measured using any suitable method. For example, wound contraction can be evaluated visually, and scar depth can be evaluated histologically. However, other techniques can be used.

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Different burn models exist. FIG. 1B illustrates a general burn model (Jackson's Burn Model) showing distinct areas of tissue damage within a burn. In FIG. 1B, the central zone of coagulation represents the zone of severe damage caused by primary injury. In general, these tissues do not recover and will eventually slough off as dead tissue over time. Surrounding the central zone of coagulation lies the zone of stasis. This zone is characterized by less damaged tissue in which inflammation occurs and vascularity is impaired. Tissue in this zone has the potential to recover under correct conditions. The outer layer is the zone of hyperaemia characterized by tissue with intense vasodilatation and increased blood flow. The margins between the zones are not static since they are influenced by local and systemic factors, including reduced blood flow. In some embodiments, excessive edema tends to extend the zone of coagulation and hence the area of tissue necrosis. Under favorable conditions, the margin of the central zone remains static and the zone of stasis shrinks as it is replaced by the zone of hyperemia. According to aspects of the invention, different burn zones can be identified by analyzing IR data from a burned tissue as described herein.

It should be appreciated that a burn wound is dynamic and subject to the effect of secondary injury. For example, the burn may deepen if the blood supply of the wound is impaired (e.g., due to hypovolaemia, hypotension, or if infection occurs).

FIGs. 2A and 3A illustrate a non-limiting examples of a burn model using pig skin, where different regions (e.g., different squares) are exposed to different temperatures for different lengths of time to provide models for different levels of burn severity. FIG. 2B shows IR emission images of the burned tissue. FIG. 2D depicts a method for analyzing IR image data and illustrates that, in some embodiments, a mathematical size or quantification of a peak or valley (e.g., area under curve) can be used to assess the extent and/or severity of a burn or wound. In some embodiments, a larger area may be the result of colder temperatures, which may be due to lower perfusion and/or indicative of greater tissue damage.

FIGs. 3B-3C show an analysis of the IR emission across several burned regions. It should be appreciated that the IR image in FIG. 3B is a different view from the visual picture of FIG. 3A. The spot location is the same as circled, but the visual picture is shown with the spine in the middle. Two different sets of data are shown at the same time. This may be more similar to an actual burned area where the degrees of burn are intermixed. FIG. 3B shows an example of IR data for day one after a burn. The data is shown as a temperature profile, but it should be appreciated that data can be evaluated and/or displayed as an IR emission profile and does not

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need to be converted into temperature. In this non-limiting example, baseline skin temperature in the burn area is 34 to 34.4 °C, temperature in the burn is about 33.2 °C, and temperature in the areas surrounding the burns is 36.1 to 36.9 °C. A histological analysis of these areas can be used to evaluate the extent of damage below the surface of the burned regions so that IR profiles for different levels of burn severity can be confirmed.

FIG. 4 shows IR data in more detail and illustrates models of a deep burn (see FIG. 4B) and a shallow burn (see FIG. 4C). It should be appreciated that deep burns may have low vascular destruction deeper down, in some embodiments. This may be reflected by a low central temperature within a few hours after a burn. In some embodiments, a difference in emission levels between different regions can be highlighted if there is no, or less, tissue healing or inflammation that can make the data more difficult to evaluate.

FIG. 5 shows a non-limiting example with several (7) distinguishable layers of tissue disruption one day after a burn as detected by different levels of IR emission. It should be appreciated that different levels of IR emission can be distinguished based on the calibration of the IR detector. FIGs. 6 and 7 show non-limiting examples of IR top-view patterns and models of different burn depth profiles. In some embodiments, the outer perimeter is cooler in the burns resulting from hotter and/or longer burning conditions relative to the outer perimeter of the burns resulting from cooler and/or shorter burning conditions. In some embodiments, IR energy comes through the tissue, but because the hotter and deeper burning conditions produce more damage and deeper damage (loss of blood flow, loss of temperature, dehydration, small inflammatory response) that may not be evident on the surface, the IR energies are absorbed differently than for shallower burns (e.g., resulting from exposure to shorter burning conditions). Accordingly, shorter and shallower burns appear overall hotter (higher IR emissions) than the deeper burns. In some embodiments, shallower burns are characterized by having a higher number of readily distinguishable levels of IR emission (e.g., a higher number of different heat levels) than deeper burns. For example, in some embodiments shallow burns have seven different layers radiating from the burn center, whereas deep burns only have six. In some embodiments, the colder outside perimeter is cooler for the deep burns than for the short and shallow burns. In some embodiments, shallow burns allow higher IR emissions (e.g., detected as temperature using an IR detector calibrated to detect temperature) to radiate from underneath the burn and be detectable at the surface through the wound.

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FIGs. 8-10 show different patterns of IR profiles and scars for different burns at different times after injury. FIG. 9A shows IR patterns of scars at 28 days after injury. FIG. 9B shows IR patterns of burned tissue at 24 hours after injury. FIG. 9C illustrates IR patterns of burned tissue at 24 hours, 72 hours, and 7 days after injury. A temperature profile is shown for both a superficial and a deep-dermal burn. The shape of the profile is similar for both superficial and deep-dermal burns, but the detected temperatures are lower for the deep dermal burns. The burn profiles are detectable at both early and later time points, although there is a detectable shift in the profiles towards higher temperatures at later times after the injury. FIG. 9D illustrates that IR data at 24 hours after injury correlates with wound contraction and scar depth 4 weeks after injury. The first panel shows IR data 24 hours after a burns of three different depths. The second panel shows the % wound contraction for these three burn types 4 weeks after the injury, and the third panel shows the scar depths for the three burn types 4 weeks after the injury. The scar depth is evaluated by histology at 4 weeks. The IR data is consistent with the physiological outcome. For example, the 70/20 burn (70 °C for 20 seconds) has a lower depth than the 80/30 burn (80 °C for 30 seconds). FIG. 9E illustrates that IR data at different times after injury correlates with scar depth 4 weeks after injury.

In FIG. 10, 14 and 15 show minimal scarring after 672 hours. However, characteristic ring destruction pattern is still evident on scarred skin, wherein minimally-scarred tissue shows little or no ring destruction.

FIG. 11 shows a high definition IR image of a day old burn. In some embodiments, in a non-scarring burn the temperature in the center is warmer than for a scarring burn, and the temperature change from the center to the outside of a non-scarring burn goes up towards the outer edge. In contrast, a scarring burn does not change temperature as much. Also, scarring burns are typically colder than an average skin temperature (even at 672 hours after a burn).

FIG. 12 provides a model for real burns based on infrared contrast imaging (IRCI) data, illustrating a shallower pattern of IR changes radiating from the center of a deep burn than for a shallow burn. FIG. 13 provides an example of an analysis of a burned tissue model and illustrates how shallow and deep burns can be identified based on patterns of IR emission (and the extent of change in IR emission from the center of a burn). In some embodiments, an analysis involves finding low emission (e.g., low temperature) spots, analyzing temperature changes in one or more directions radiating from the low spots (e.g., in 1, 2, 3, 4, or more directions, for example NSEW directions, or along any other relative directions), and

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determining the rate of change (e.g., the slope of one or more radiating vectors or using any other suitable analysis). In some embodiments, the areas with the flattest slopes from the coolest areas will identify regions of deep burns, whereas areas with the greatest slope changes will represent shallow burns. It should be appreciated that areas that overlap can be determined as to degree of scarring with a suitable calibration curve in some embodiments.

FIG. 14 illustrates vectors representing patterns of IR emission changes from the centers of burned regions that can be used to evaluate burn depth (and, for example, to distinguish shallow burns from deep burns). In some embodiments, steps for evaluating tissue damage, for example burn severity, include one or more of a) finding a center of lowest emission (e.g., lowest temperature), b) measuring a diameter through the coldest area (shallow burns are hotter, and deeper burns are colder); and c) measuring ring areas of IR emissions (e.g., temperatures - shallow burns have higher temperatures and more rings at higher temperatures, whereas deeper burns are colder). Accordingly, in some embodiments, a burn can be evaluated by determining the diameter, surface area, or other measure for one or more (e.g., two or more) different levels of IR emission for different regions of a burn and comparing these measurements to determine the relative burn severity of the different regions. In some embodiments, if skin temperature is measured at around 32 °C, then scarring does not occur.

FIG. 15 illustrates non-limiting examples of IR emission profiles (shown as temperature profiles) across the diameter of a burn. This illustrates how IR emission profiles can be used to help evaluate burns early. This is a significant problem, because when a person is burnt, the burn visually looks similar for about two weeks but at the end of that time there are deep burns that scar and shallow burns that heal with minimal to no scarring. Since burns cannot be visually evaluated early on to distinguish regions of deep burn from regions of shallow burn, specific or targeted treatments cannot be applied before the end of two weeks. By that time, a deep burn can be cleaned, but the scarring will be bad. In contrast, an IRCI image of a burn can be used to rapidly (and soon after injury) between deep (on top of figure) and shallow (on bottom of figure) burns. For example, there are distinct differences that are apparent from about 3 hours after the burn to about 48 hours after the burn. After that there are still differences that can be identified, but they are not as clear. In some embodiments, both shallow and deep burns have lowest levels of IR emission (lowest temperatures) at their centers (or in the region of highest tissue damage). However, badly burnt tissue will have lower levels of emission (e.g., a colder middle) and a lower rate of IR emission change (e.g., temperature change) as a function

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of distance radiating out from the center. In contrast, shallow burns have a higher middle temperature than deep burns (but still lower than normal skin temperature) and the slope of the increase from the center is much greater than for deep burns.

FIG. 16 illustrates non-limiting examples of vectors radiating from the points of lowest emission for shallow and deep burns. In some embodiments, intersections of shallow and deep burns can be determined (e.g., by calculation or image analysis). In some embodiments, this allows for an overlay (e.g., a transparent and/or color overlay) to be prepared (e.g., printed). For example, with one or more physical reference points that can be used to match the images up with the burnt tissue of a subject so that a surgeon or medical practitioner could pick away severely burnt tissue, or otherwise selectively treat tissue as a function of burn severity, under the overlay. In some embodiments, an overlay can be projected or otherwise displayed on the surface of a patient's skin to indicate the relative and/or specific levels of burn for different regions, thereby allowing a surgeon or other medical practitioner to apply different appropriate treatments to different regions based on their burn severity.

This technique of using a printed or projected patterns to assist a physician or medical practitioner can be used for other injuries or conditions (e.g., skin injuries or conditions). In some embodiments, one or more reference points are provided along with the IR pattern to allow the printed or displayed pattern to be aligned with a subject. Different techniques can be used to generate one or more reference points. In some embodiments, a reference point can be a body feature (e.g., a joint or other identifiable body feature). In some embodiments, one or more reference points can be added to the tissue prior to obtaining the IR data. For example, one or more spots of a dye or other material that either increases or reduces an IR signal can be used. In some embodiments, a drop of water can be used to provide a mark due to decrease IR signal. In some embodiments, the drop of water contains a dye or other marker that is left on the skin at the site of the drop. This can be used later to align the printed or displayed pattern by aligning the IR reference spot corresponding to the drop of water with the dye spot on the skin. It should be appreciated that other techniques for producing and using one or more reference points can be used to spatially align or register patterns for treatment as aspects of the invention are not limited in this respect.

FIG. 17A illustrates further non-limiting examples of vectors radiating from the points of lowest emission for several shallow and deep burns. Accordingly, calculations or other analyses can be performed to create a map of different levels (e.g., different relative levels) of burn.

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Depending on the extent of a burn and/or the location of a burn, different levels of spatial resolution can be used. For example, FIG. 17B illustrates a non-limiting example of a profile obtained from an IR image containing an irregular burn pattern.

Accordingly, methods described herein can be used to evaluate burned tissue early, for example before visual differences can be identified between shallow and deep burns. This allows for earlier and more effective therapeutic intervention. Similar techniques can be used to evaluate other tissue injuries and/or conditions as described herein.

It should be appreciated that aspects of the invention are based on the natural emissivity of tissue and differences in emissivity caused by injury or disorders. Accordingly, no markers, dyes, or other detectable agents are required in some embodiments. Similarly, Doppler or other acoustic techniques also are not required in some embodiments. However, it also should be appreciated that aspects of the invention can be combined with other techniques that involve Doppler and/or other acoustic techniques and/or detectable markers.

In some embodiments, the levels of tissue emissivity, and, in particular, differences in the levels of emissivity that are associated with different types or degrees of injury can be detected using an infrared detection device that is calibrated to maximize the contrast between different tissue appearances rather than being calibrated to detect the temperature of a tissue. Accordingly, IR contrast imaging can be performed by calibrating an IR detector to be most sensitive to contrasts between different IR levels that are associated with an injury or condition. In some embodiments, a high resolution palette can be used to display different levels of IR emission that may not be distinguishable using typical display palettes that do not provide sufficient contrast (e.g., between IR levels corresponding to physiological injuries or conditions, for example, corresponding to 0-50 °C, around 25-50 °C). However, aspects of the invention are not limited in this respect, and information that is obtained using a device (e.g., camera) that is calibrated to detect temperature levels also can be analyzed to evaluate the extent of tissue injury.

In some embodiments, a tissue can be the tissue of a human subject. However, a tissue of an animal (e.g., a vertebrate, invertebrate, mammal, or other subject) can be evaluated using techniques described herein. In some embodiments, the subject has been injured and techniques described herein are used to evaluate the extent of the injury. Accordingly, methods described herein can be used to determine whether and/or how to treat a subject based on the presence or extent of injuries detected. In some embodiments, the tissue is skin. However, in some

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embodiments, the tissue is mucosal tissue, eye tissue (e.g., corneal tissue, or other ocular tissues), or an internal tissue such as, fascia or another connective tissue.

In some embodiments, a pattern of differences in infrared emissions can be used to establish an extent and/or pattern of tissue injury. This information can be used to determine a course of therapy for the injured tissue. In some embodiments, different types of therapy may be recommended based on the level or extent of injury.

In some embodiments, a pattern of injury (e.g., based on an infrared pattern) of a tissue that is determined using techniques described herein can be displayed on a subject in order to precisely target a therapy to the appropriate tissue region. In some embodiments, different therapies are applied or targeted to different regions of injured tissue based on the level of injury determined using techniques described herein. By displaying the pattern of injury on the subject (e.g., using a projector, or other technique), levels or types of treatment can be precisely targeted. However, it should be appreciated that instead of directly displaying a pattern on the subject, the pattern can be displayed on a screen or photo or other medium that a physician can use to select and/or target one or more treatments to the appropriate injury regions.

In some embodiments, one or more physical reference points are provided along with the injury pattern. Reference points can be body regions (e.g., joints such as elbows, knees, or hips, extremities such as fingers or toes, the head or features on the head such as the nose or ears, or other body parts). In some embodiments, one or more physical markers can be applied to body regions (e.g., colored markers, water spots, other liquid spots, etc.) near the site of an injury and the position of the marker(s) relative to the injury pattern can be determined and used in therapy. For example, one or more natural or artificial reference points can be used to precisely locate on a subject the different levels of injury that were identified using methods described herein. This can be useful for targeting therapy, for example, in instances where large extents of tissue are injured (e.g., burned) and it can be difficult to determine how to treat different parts of the injured (e.g., burned regions).

In some embodiments, patterns of injury can be determined based on the contrast (e.g., infrared contrast, for example, far infrared contrast) between different parts of an injured tissue. In some embodiments, it is not the absolute level of emission that is used to determine injury patterns, rather the differences in emission between different regions are useful to determine relative levels of injury. However, in some embodiments, reference levels of emission can be established for normal and/or different levels of injury. It should be appreciated that reference

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levels may be different for different parts of the body and for different individuals (e.g., based on different ages and/or other physical traits). However, as discussed above, the relative emission levels for any individual can be used to determine injury patterns. In some embodiments, a normal level can be established for an individual based on levels of emission detected for undamaged tissue in the individual. Accordingly, an emission pattern can be established for a region expected to be injured and also for surrounding regions. In some embodiments, the pattern is detected for a large region in order to ensure that non-injured tissue is included in the analysis. However, non-injured tissue is not always required. As discussed herein, the contrast between different tissue regions can be used to determine a pattern of injury.

In some embodiments, different emissions (e.g., different infrared emissions) from a tissue region can reflect surface tissue damage. However, it also should be appreciated that tissue damage at different depths from the tissue surface also can change the emission patterns (e.g., infrared emission patterns). Accordingly, patterns of emission changes (e.g., contrasts in emission levels) can be used to evaluate surface and or deeper tissue injuries. In some embodiment, the techniques herein are used to evaluate the extent of an injury to skin or another tissue. For example, in some embodiments, the techniques are used to determine the depth of a skin injury, e.g., whether a skin injury is limited to epidermal tissue or extends into or through dermal tissue or into or through basement membrane.

In some embodiments, aspects of the invention are useful for detecting injuries and/or evaluating the extent and/or severity of an injury before other physical signs (e.g., visual signs such as bruising, blistering, etc., or any combination thereof) are detectable. This allows injuries to be detected and/or evaluated earlier. These injuries can therefore be treated earlier. This can provide significant benefits associated with early treatment and/or triage of patients after an accident or other traumatic event.

In certain embodiments, aspects of the invention allow for more precise treatments to be targeted to different regions of an injury based on different levels of injury detected using infrared emission patterns detected from the tissue.

Accordingly, in some embodiments a method of evaluating, or assisting in the evaluation of an injury (e.g., a burn) in a subject includes detecting infrared emission from a tissue region (e.g., a burn) in a subject, and determining a pattern of infrared emission levels for the tissue region (e.g., burn).

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In some embodiments, the infrared emission is detected less than 72 hours (e.g., less than 48 hours, less than 24 hours, less than 12 hours, less than 6 hours, less than 3 hours, less than 1 hour, less than 30 minutes, less than 15 minutes, less than 10 minutes, or less than 5 minutes) after an event that caused the tissue injury (e.g., burn) in the subject. However, it should be appreciated that techniques described herein are not limited to detecting short term tissue damages or changes, but can also be used to detect and evaluate long term damage and/or tissue changes.

In some embodiments, the injury should be cooled prior to obtaining IR data. For example, if the injury is associated with heat (e.g., a burn), the heat from the injury itself (e.g., the heat of the burn itself) can obscure the IR patterns or profiles associated with changes in the emissivity of the tissue caused by the injury. For example, a solution or saline could be applied to the area of suspected of being injured prior to obtaining IR data. The solution could be water or a saline solution or any other solution at any suitable temperature (e.g., cold, cool, room temperature, or body temperature, for example).

In some embodiments, the event that caused the tissue burn was an exposure to heat, an exposure to a chemical element, or an exposure to radiation. In some embodiments, the tissue burn is a skin burn.

In some embodiments, infrared emission is detected from a tissue region that includes injured (e.g., burnt) tissue and tissue surrounding the injured tissue, and wherein the pattern of infrared emission levels includes both the injured tissue and the surrounding tissue. In some embodiments, the surrounding tissue includes a region of tissue that is at the margin of the injured (e.g., burnt) tissue and that is at least 0.5 cm, 1 cm, 5 cm, or more wide.

In some embodiments, the infrared radiation emission that is detected is a far infrared radiation emission. In some embodiments, the far infrared wavelengths detected are 15-1,000 μm .

In some embodiments, the pattern is a two-dimensional pattern of emission levels, e.g., a pattern of emission levels measured over time across an area. In some embodiments, the pattern is a three-dimensional pattern of emission levels, e.g., a pattern of emission levels measured over time from a volume, or a pattern of emission levels within a volume of tissue.

In some embodiments, a method of evaluating a burn further comprises evaluating the emission pattern to identify one or more different levels of burn severity within the tissue burn. In some embodiments, the different levels of burn severity correspond to different burn degrees.

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In some embodiments, the different levels of burn severity correspond to different burn depths. In some embodiments, the different levels of burn severity are indicative of different degrees of tissue injury associated with different therapeutic treatments. In some embodiments, the different levels of burn severity are discrete levels. In some embodiments, the different levels of burn severity represent a continuous gradation of burn severity.

In some embodiments, an infrared emission pattern is indicative of, a) a heat pattern within the injured (e.g., burnt) tissue; b) a pattern of density variation within the tissue (e.g., vascular density); c) a hydration pattern within the injured (e.g., burnt) tissue, and/or; d) a pattern of tissue surface variation over the injured (e.g., burnt) tissue.

In some embodiments, the pattern of density variation represents density changes associated with the burnt tissue. In some embodiments, the pattern of tissue surface variation represents tissue surface changes associated with the burnt tissue.

In some embodiments, the slope of infrared emission change between a first region in the injured (e.g., burnt) tissue and a second region in the tissue (e.g., injured tissue) is determined. In some embodiments, the first region is a region of low emission. In some embodiments, a profile of relative infrared emission levels is determined across a line segment (e.g., a stretch of connected pixels) spanning a portion of 2D or 3D image of a tissue or surface, e.g., as depicted in FIG. 3. In some embodiments, the line segment spans multiple regions of the tissue or surface having different infrared emission characteristics and the different characteristics are analyzed to identify areas of damaged tissue or surface aberrations of an object.

In some embodiments, an appropriate therapeutic treatment is recommended/selected based on the infrared emission pattern of the injured (e.g., burnt) tissue. In some embodiments, an appropriate therapeutic treatment is administered based on the infrared emission pattern of the injured (e.g., burnt) tissue. In some embodiments, a first therapeutic treatment is recommended/selected for a first region of the injured (e.g., burnt) tissue and a second therapeutic treatment is recommended/selected for a second region of the injured (e.g., burnt) tissue, based on different levels of infrared emission from the first and second regions of the injured tissue.

In some embodiments, a first therapeutic treatment is selected for a first region of the burnt tissue and a second therapeutic treatment for a second region of the burnt tissue, based on different levels of infrared emission from the first and second regions of the burnt tissue.

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In some embodiments, a therapeutic treatment comprises removing burnt tissue. In some embodiments, the first therapeutic treatment comprises removing tissue from the first region of burnt tissue. In some embodiments, the depth of burnt tissue that is removed is based on the level of infrared emission. In some embodiments, the depth of tissue that is removed from the first region is based on the level of infrared emission from the first region.

In some embodiments, the first therapeutic treatment comprises administering a first compound to the first injured (e.g., burnt) region. In some embodiments, the second therapeutic treatment comprises administering a second compound to the second injured (e.g., burnt) region.

In some embodiments, first and second compounds (and/or first and second levels of a similar or identical compound) are provided on a solid support (e.g., a bandage) and the pattern of the first and second compounds on the bandage corresponds to the pattern of the first and second injured (e.g., burnt) regions on the subject. It should be appreciated that more than two levels or types of therapeutic compounds can be provided on a solid support in a pattern that corresponds to a pattern of more than two levels of tissue injury detected for a subject.

In some embodiments, aspects of the invention relate to a bandage comprising a first region having a first therapeutic compound for treating an injury (e.g., a burn), and a second region having a second therapeutic compound for treating an injury (e.g., a burn), wherein the first and second regions are configured in a pattern on the bandage that corresponds to a pattern of different levels of injured tissue associated with a subject. In some embodiments, the bandage comprises a pattern of three or more different regions each having a different therapeutic compound, wherein the pattern of the different therapeutic compounds on the bandage corresponds to a pattern of different levels of injured tissue associated with an injury on a subject.

In some embodiments, aspects of the invention relate to a bandage (or other medical application), that can have a pattern of burn/wound severity printed out on at least one surface corresponding to a particular burn or wound so that it can be placed on the burn or wound. Reference points can be marked on a patient and used to align the printed bandage. In some embodiments, the bandage can have a decellularizing ink (e.g., SDS, or other decellularizing compound or mixture) or other debriding composition that can be printed in a concentration matching the severity of the burn or wound. Accordingly, this can dissolve tissue in a specific pattern that corresponds to the burn or wound severity. In some embodiments, a bandage will trap softened tissue in its structure and, when removed, take tissue off in proportion to the

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severity of the burn or wound and its spatial locations. In some embodiments, another bandage can be printed with a treatment and/or cells to be delivered to specific portions of a burn. In some embodiments, a separate device can be used to spray or otherwise deliver treatments and/or graft cells onto exposed areas. In some embodiments, physical reference points can be used to align bandages (or target other treatments) as a function of levels of tissue damage as determined by IR analysis.

Similarly, other treatments (e.g., one or more antibiotics, antimicrobials, anti-inflammatories, cytotoxic, anti-cancer, anti-oncogenic, palliative, oxidizing agents, peroxide, hydrogen peroxide, therapeutic drugs, neomycin, or other compounds, or combinations thereof) can be printed on bandages in one or more spatial patterns that correspond to IR patterns (e.g., as illustrated in FIG. 18) in order to treat wounds, burns, infections, frostbite, gangrene, skin cancer, skin disorders (e.g., a callus or a corn) or other conditions. In some embodiments, different compositions are provided on a single bandage (or other support material). In some embodiments, different levels (e.g., amounts or concentrations) of one or more compositions are provided on a single bandage (or other support material) in a pattern that corresponds to an injury, disease, or disorder pattern (e.g., corresponding to the extent and/or severity). In some embodiments, a printer can be used to print multiple or single preparations in a spatial relationship that corresponds to an IR pattern or other imaging techniques. These can be used to provide spatially accurate images of damage and/or provide treatments in spatially accurate position to prepare, treat, and/or heal different levels of injury simultaneously. Accordingly, in some embodiments, a method of producing a bandage comprising a spatial configuration of one or more compositions comprises obtaining IR data for a target tissue (e.g., injured or diseased), processing the data to determine a pattern of compositions or levels of composition (e.g., treatment) that are adapted to the pattern of the tissue (e.g., skin) injury or disorder determined from the IR data, and preparing a bandage or other support with the pattern of compositions or levels of composition (e.g., using a printer).

In some embodiments, water, biological solutions (e.g., blood, saliva, etc., or any combination thereof), buffers, etc., or any combination thereof can be used as external coverings or coatings for a wound or burn, for example, to enhance the detection or different levels of IR emission (e.g., from hot or cold areas) or differences within an area.

In some embodiments, the pattern of infrared emission levels will be used as a virtual image to monitor the depth and extent of burn wound debridement.

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In some embodiments, the pattern of infrared emission levels will be used as a virtual image to monitor the depth and extent of burn injury in a clinical trial.

In some embodiments, project analysis information on wound can be aligned with reference points marked on patient. Treatment can be dictated by the spatially accurate and analyzed data.

Aspects of methods for evaluating IR image data disclosed herein may be implemented in any of numerous ways. For example, the various methods or processes outlined herein may be coded as software that is executable on one or more processors that employ any one of a variety of operating systems or platforms. Such software may be written using any of a number of suitable programming languages and/or programming or scripting tools, and also may be compiled as executable machine language code or intermediate code that is executed on a framework or virtual machine. The MATLAB image processing toolbox (The MathWorks, Inc., Natick, MA) is an exemplary, but non-limiting, system that may be used for implementing certain aspects of the methods disclosed herein.

In this respect, aspects of the invention may be embodied as a computer readable medium (or multiple computer readable media) (e.g., a computer memory, one or more floppy discs, compact discs, optical discs, magnetic tapes, flash memories, circuit configurations in Field Programmable Gate Arrays or other semiconductor devices, or other tangible computer storage medium) encoded with one or more programs that, when executed on one or more computers or other processors, perform methods that implement the various embodiments of the invention discussed herein. The computer readable medium or media can be transportable, such that the program or programs stored thereon can be loaded onto one or more different computers or other processors to implement various aspects of the present invention as discussed above.

The terms "program" or "software" are used herein in a generic sense to refer to any type of computer code or set of computer-executable instructions that can be employed to program a computer or other processor to implement various aspects of the present invention as discussed above. Additionally, it should be appreciated that according to one aspect of this embodiment, one or more computer programs, which when executed perform certain methods disclosed herein, need not reside on a single computer or processor, but may be distributed in a modular fashion among or between a number of different computers or processors to implement various aspects of the present invention.

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Computer-executable instructions may be in many forms, such as program modules, executed by one or more computers or other devices. Generally, program modules include routines, programs, objects, components, data structures, etc. that perform particular tasks or implement particular abstract data types. Typically the functionality of the program modules may be combined or distributed as desired in various embodiments.

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CLAIMS

What is claimed is:

1. A method of evaluating a burn, a wound, or a natural biological state of one or more cells, tissues, organs, organ systems, or objects, the method comprising:
detecting infrared emission from a tissue burn/wound, cell, tissue, organ, system, or object; and,
determining a pattern of infrared emission levels.
2. The method of claim 1, wherein the infrared emission is detected less than 72 hours after an event that caused an injury in the subject.
3. The method of claim 1, wherein the infrared emission is detected less than 48 hours after an event that caused an injury in the subject.
4. The method of claim 1, wherein the infrared emission is detected less than 24 hours after an event that caused an injury in the subject.
5. The method of claim 1, wherein the infrared emission is detected less than 12 hours after an event that caused an injury in the subject.
6. The method of claim 1, wherein the infrared emission is detected less than 6 hours after an event that caused an injury in the subject.
7. The method of claim 1, wherein the infrared emission is detected less than 3 hours after an event that caused an injury in the subject.
8. The method of any one of the preceding claims, wherein the injury is a tissue burn or a skin burn.
9. The method of any one of the preceding claims, wherein the event that caused the wound or tissue burn was an exposure to heat, an exposure to a chemical element, an exposure

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to radiation, or an exposure to a physical trauma.

10. The method of claim 9, wherein infrared emission is detected from a tissue region that includes injured tissue and tissue surrounding the injured tissue, and wherein the pattern of infrared emission levels includes both the injured tissue and the surrounding tissue.

11. The method of claim 10, wherein the surrounding tissue includes a region of tissue that is at the margin of the injured tissue and that is at least 0.5 cm, 1cm, 5 cm, or more wide.

12. The method of any of the preceding claims, wherein near, mid, and/or far infrared radiation emission is detected.

13. The method of any one of the preceding claims, wherein the infrared radiation emission that is detected is a far infrared radiation emission.

14. The method of claim 13, wherein the far infrared wavelengths detected are 15-1,000 μm .

15. The method of claim 1, wherein the pattern is a two-dimensional pattern of emission levels.

16. The method of claim 1, wherein the pattern is a three-dimensional pattern of emission levels.

17. The method of claim 1, further comprising evaluating the emission pattern to identify one or more different levels of injury severity within the injured tissue.

18. The method of claim 17, wherein the different levels of injury severity correspond to different burn degrees.

19. The method of claim 17, wherein the different levels of injury severity

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correspond to different burn depths.

20. The method of claim 17, wherein the different levels of injury severity are indicative of different degrees of tissue injury associated with different therapeutic treatments.

21. The method of claim 17, wherein the different levels of injury severity are discrete levels.

22. The method of claim 17, wherein the different levels of injury severity represent a continuous gradation of burn severity.

23. The method of claim 1, wherein the infrared emission pattern is indicative of:

- a. a heat pattern within an injured tissue,
- b. a pattern of density variation within the tissue (e.g., vascular density)
- c. a hydration pattern within an injured tissue, and/or
- d. a pattern of tissue surface variation over an injured tissue.

24. The method of claim 23, wherein the pattern of density variation represents density changes associated with the injured tissue.

25. The method of claim 23, wherein the pattern of tissue surface variation represents tissue surface changes and/or deeper tissue changes associated with the injured tissue.

26. The method of claim 1, comprising determining the slope of infrared emission change between a first region in the tissue injury and a second region in the tissue injury.

27. The method of claim 26, wherein the first region is a region of low emission.

28. The method of claim 1, wherein an appropriate therapeutic treatment is recommended/selected based on the infrared emission pattern of the injured tissue.

29. The method of claim 1, further comprising administering an appropriate

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therapeutic treatment based on the infrared emission pattern of the injured tissue.

30. The method of claim 1, wherein a first therapeutic treatment is recommended/selected for a first region of the injured tissue and a second therapeutic treatment is recommended/selected for a second region of the injured tissue, based on different levels of infrared emission from the first and second regions of the injured tissue.

31. The method of claim 1, further comprising selecting a first therapeutic treatment for a first region of the injured tissue and a second therapeutic treatment for a second region of the injured tissue, based on different levels of infrared emission from the first and second regions of the injured tissue.

32. The method of claim 28 or 29, wherein the therapeutic treatment comprises removing the injured tissue.

33. The method of claim 30 or 31, wherein the first therapeutic treatment comprises removing tissue from the first region of injured tissue.

34. The method of claim 32, wherein the depth of injured tissue that is removed is based on the level of infrared emission.

35. The method of claim 33, wherein the depth of tissue that is removed from the first region is based on the level of infrared emission from the first region.

36. The method of claim 30 or 31, wherein the first therapeutic treatment comprises administering a first compound to the first injured region.

37. The method of claim 36, wherein the second therapeutic treatment comprises administering a second compound to the second injured region.

38. The method of claim 37, wherein the first and second compounds are providing on a solid support (e.g., a bandage) and wherein the pattern of the first and second compounds

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on the bandage corresponds to the pattern of the first and second injured regions on the subject.

39. The method of any prior claim wherein the injured tissue is a burned tissue, for example, a burned skin region.

40. A bandage comprising a first region having a first therapeutic compound for treating a condition, and a second region having a second therapeutic compound for treating a condition, wherein the first and second regions are configured in a pattern on the bandage that corresponds to a pattern of different levels of condition on a subject tissue.

41. The bandage of claim 40, comprising a pattern of three or more different regions each having a different therapeutic compound, wherein the pattern of the different therapeutic compounds on the bandage corresponds to a pattern of different levels of condition on a subject tissue.

42. The bandage of claim 40 or 41, wherein the condition is a burn, a wound, or a disease.

43. The bandage of claim 40 or 41, wherein the condition is acne or psoriasis.

44. The bandage of claim 42, wherein the disease is an infection or cancer.

45. The bandage of any one of claims 39-44, wherein the pattern of each of one or more therapeutic compounds is printed on the bandage.

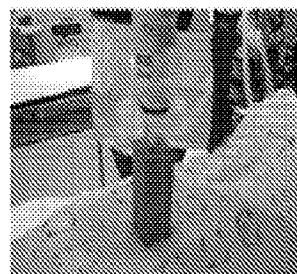
46. The method of any of claims 1-38, wherein an IR pattern is displayed using a high resolution palette.

47. The method of claim 46, wherein the high resolution palette is provided for an IR range corresponding to temperatures between or including 0-50 °C, 10-50 °C, 25-40 °C, 18-37 °C, or 25-37 °C.

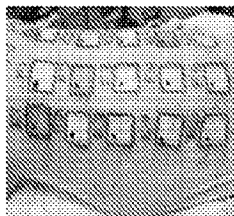
1/26

FIG 1A

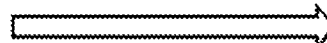
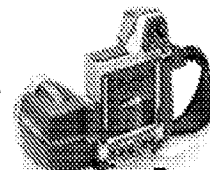
Burns created using a
hot bar



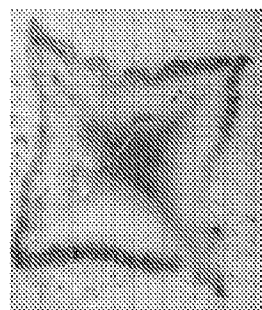
Burns



FLIR imaging



FLIR thermal
image



Outcomes:

- Wound contraction
(visual)
- Scar depth
(histology)

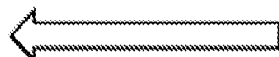


Image data
compared with
outcomes (e.g.,
at 4 weeks)

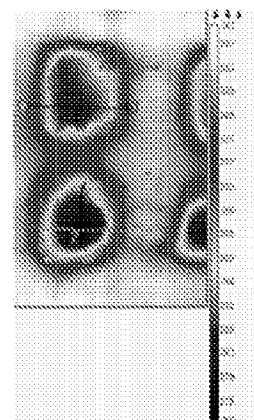


FIG 1B

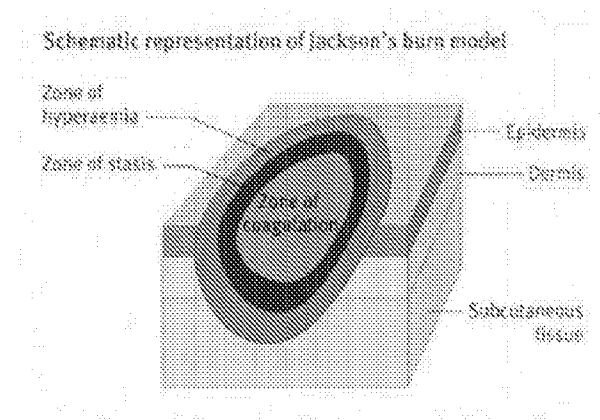
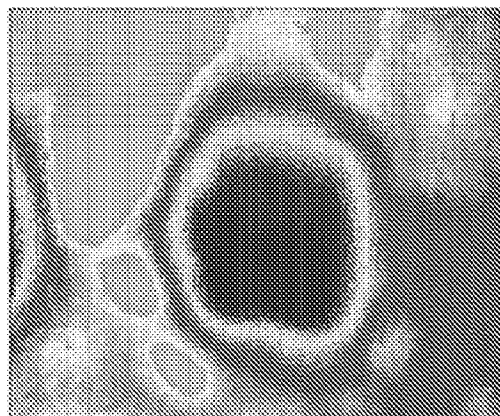


FIG 1C



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FIG 2A

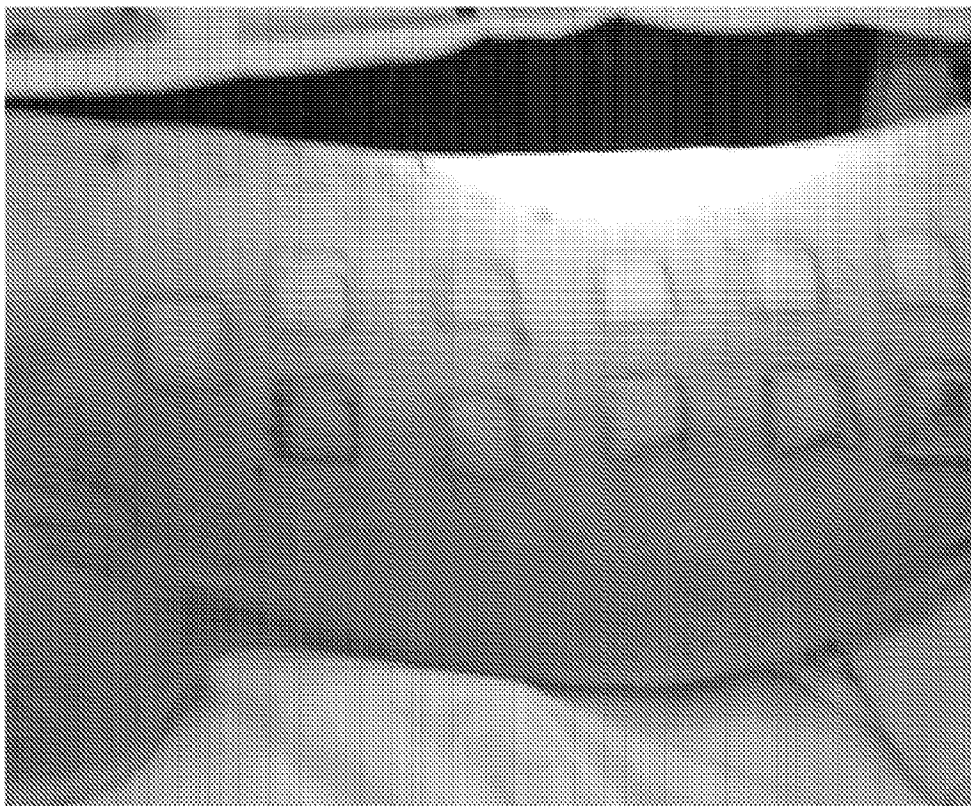
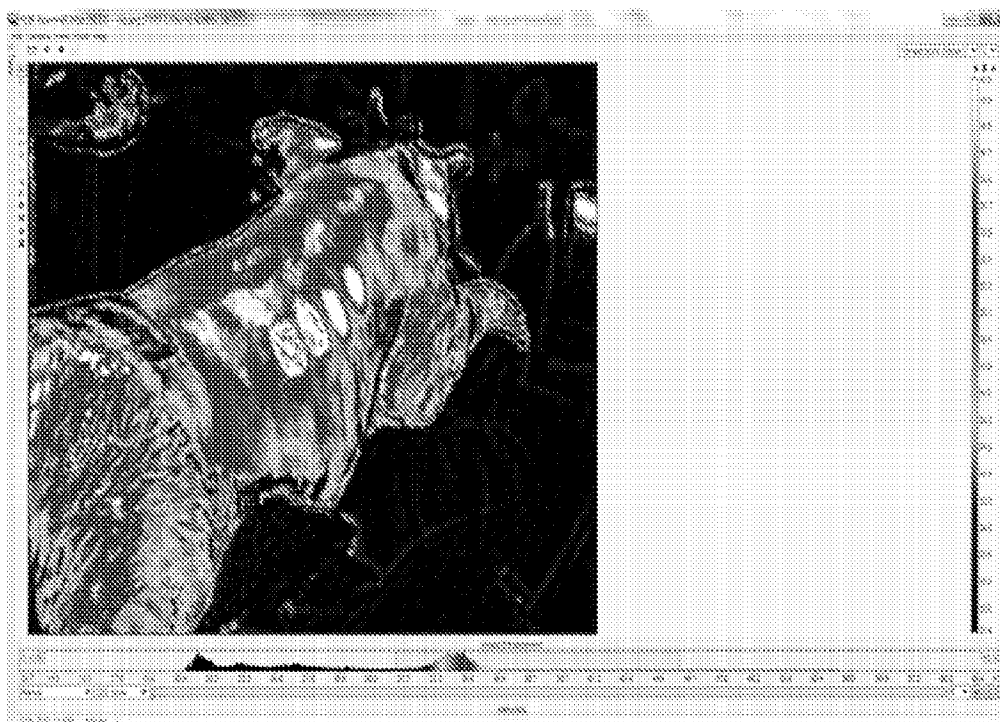


FIG 2B



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FIG 2C

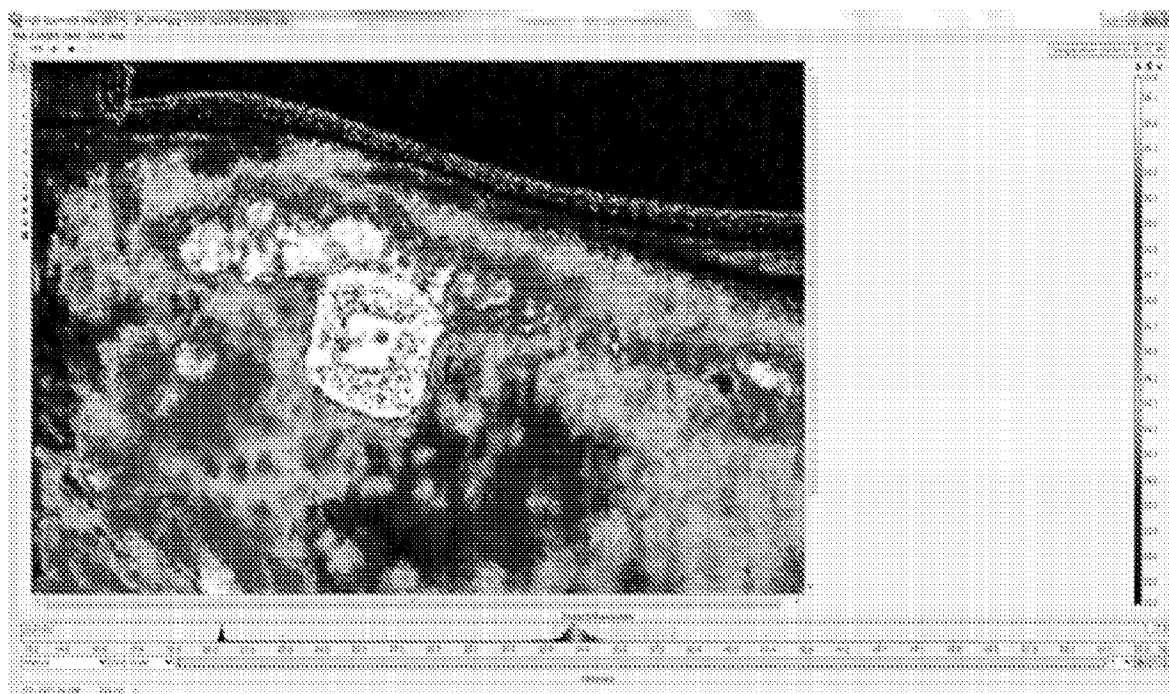
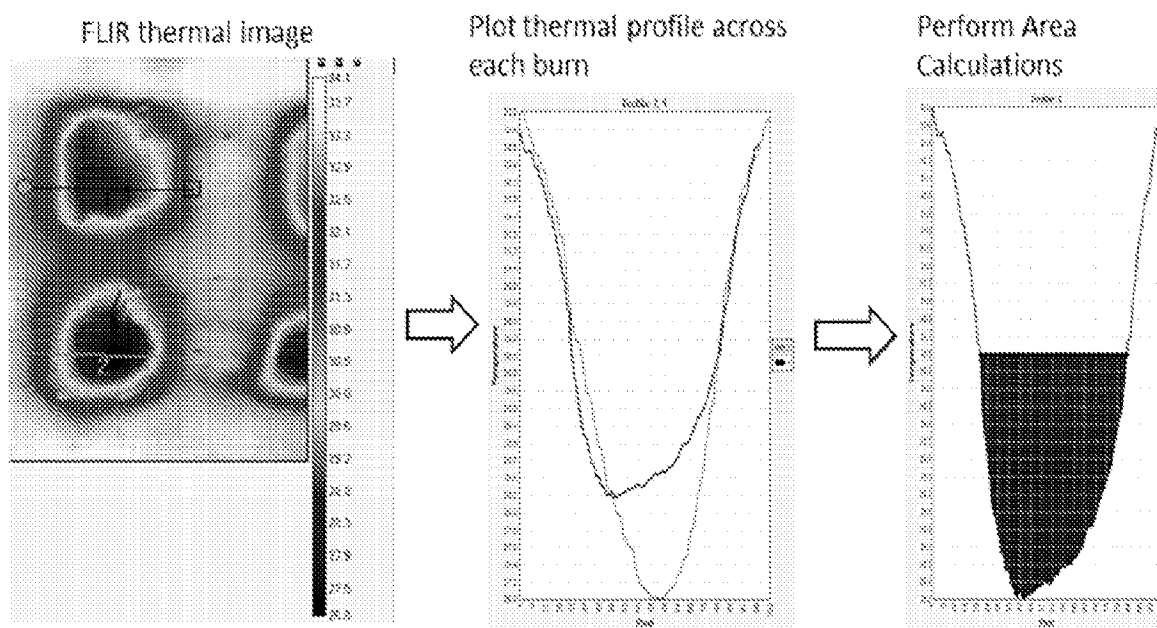


FIG 2D



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FIG 3A

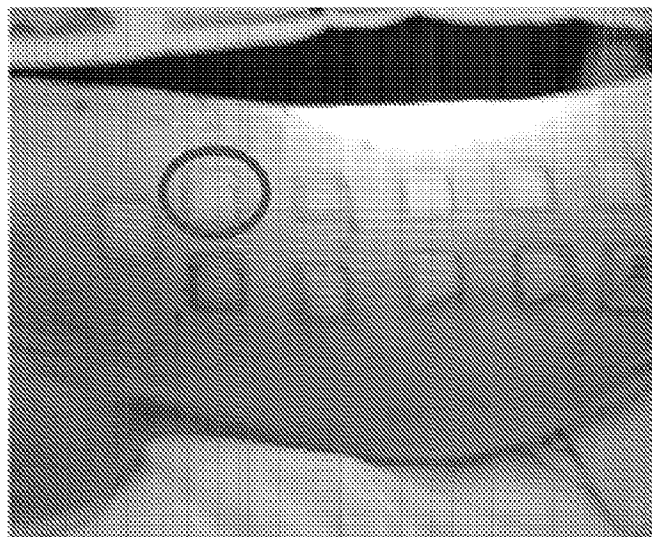
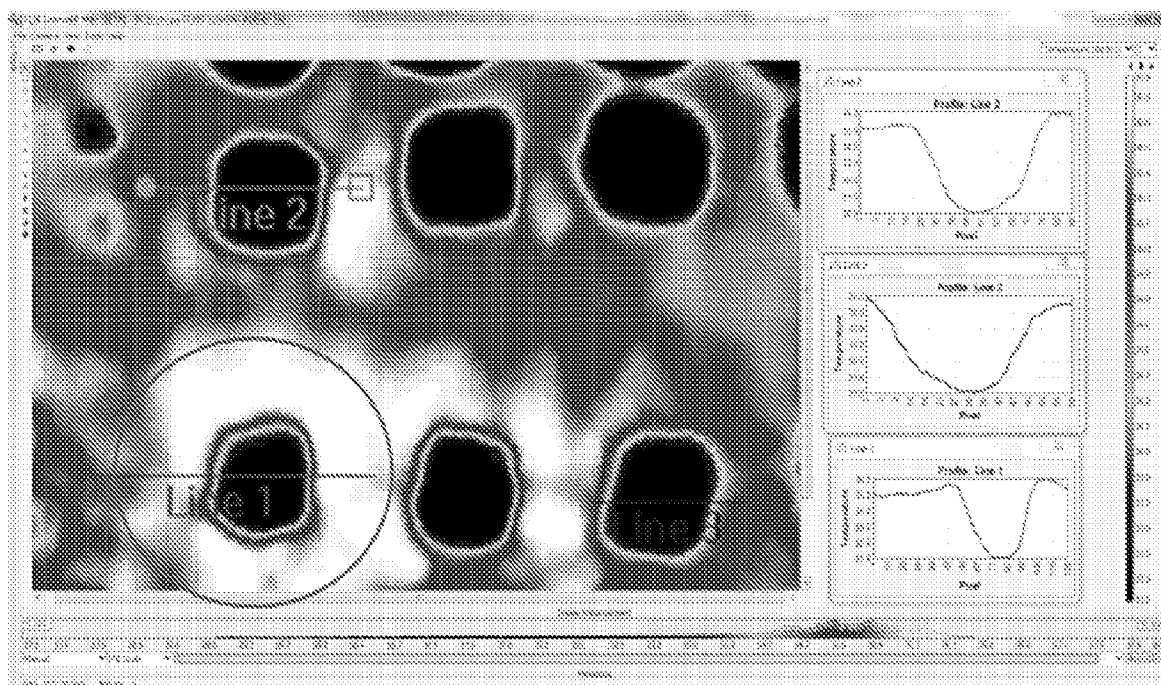
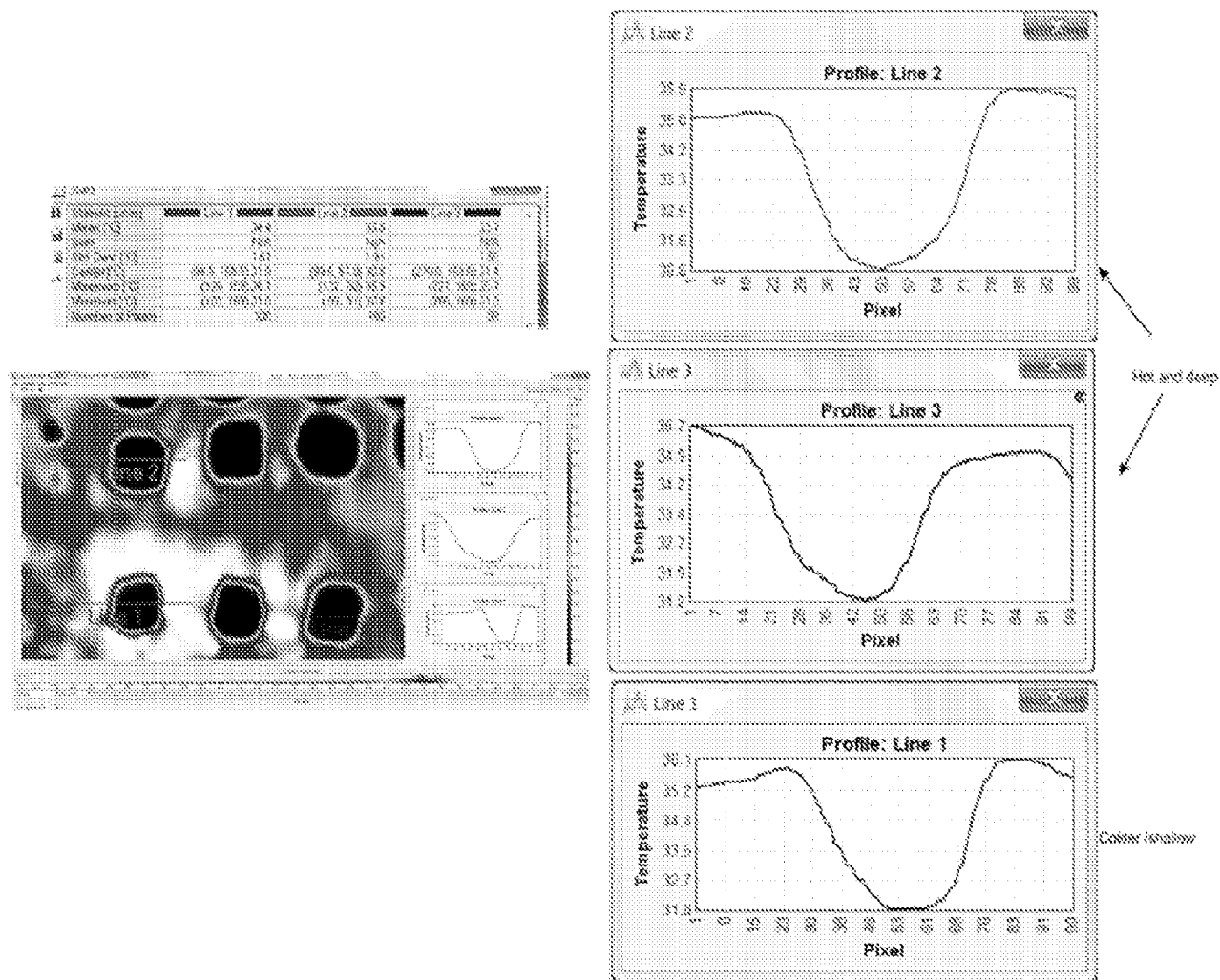


FIG 3B



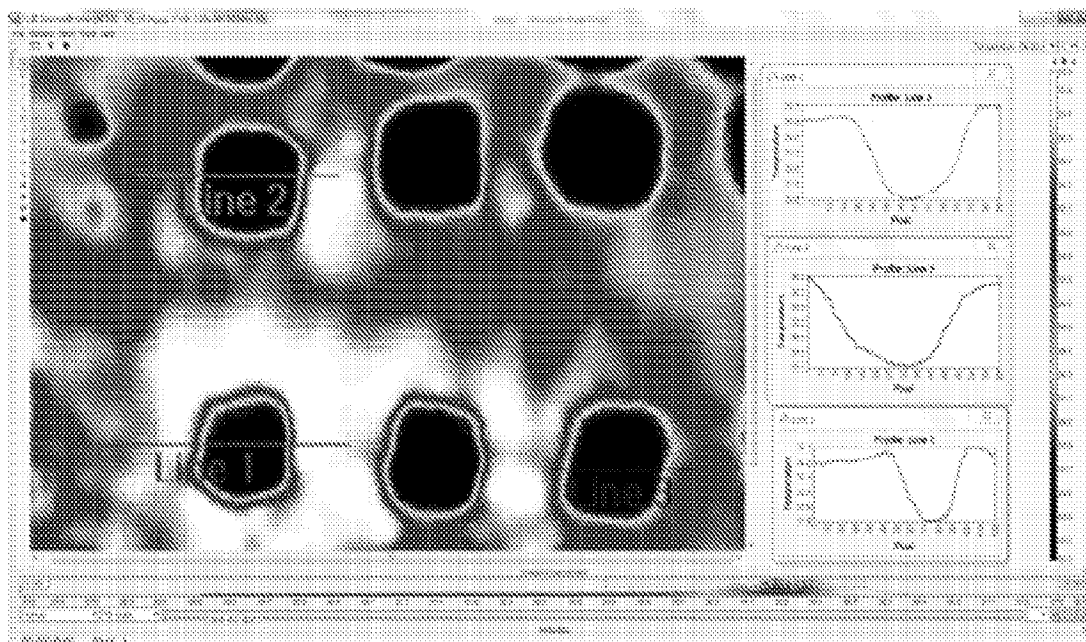
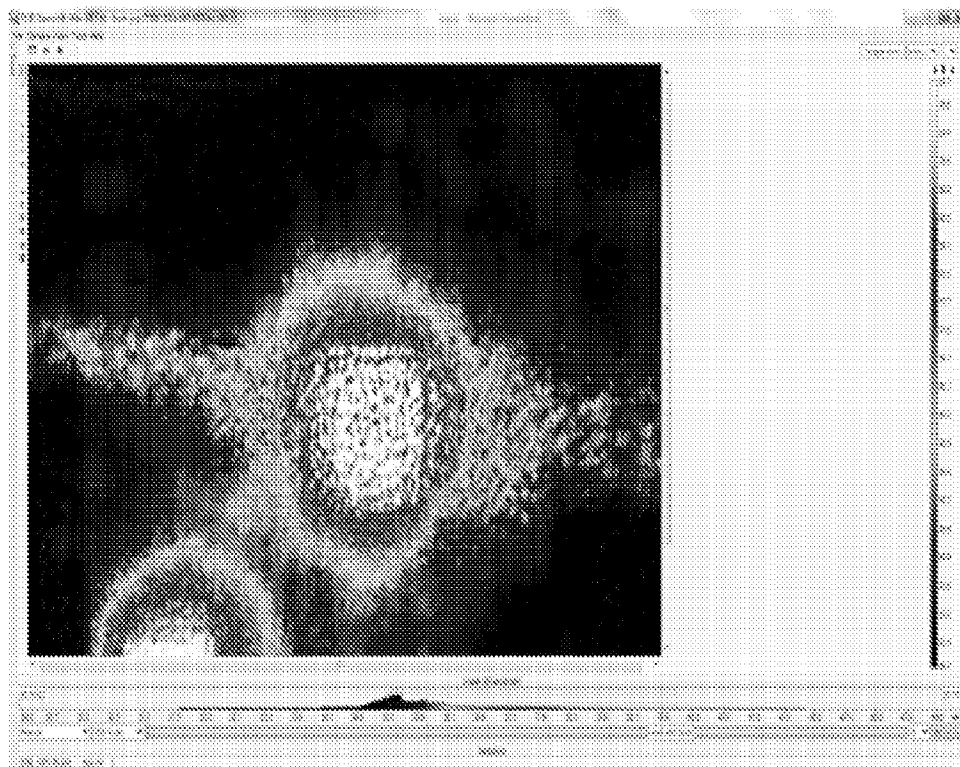
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FIG 3C



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FIG 4A



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FIG 4B

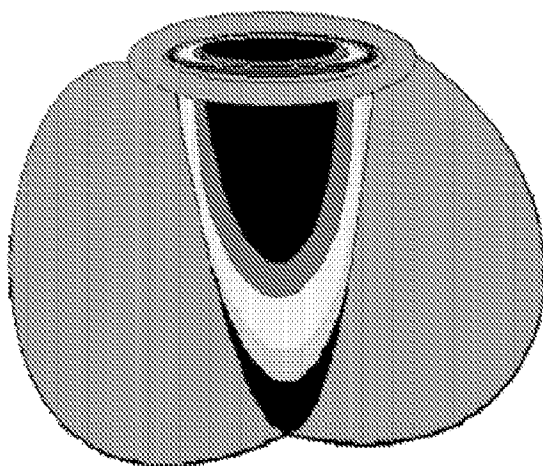
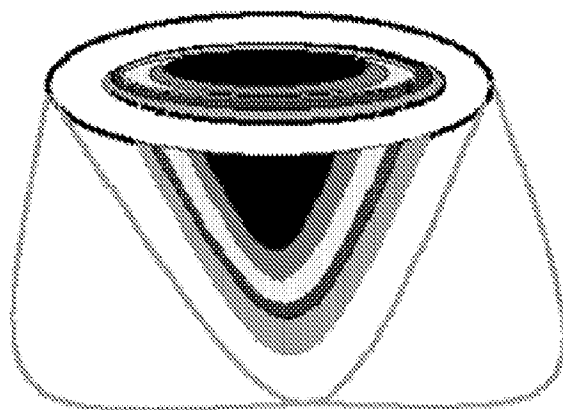


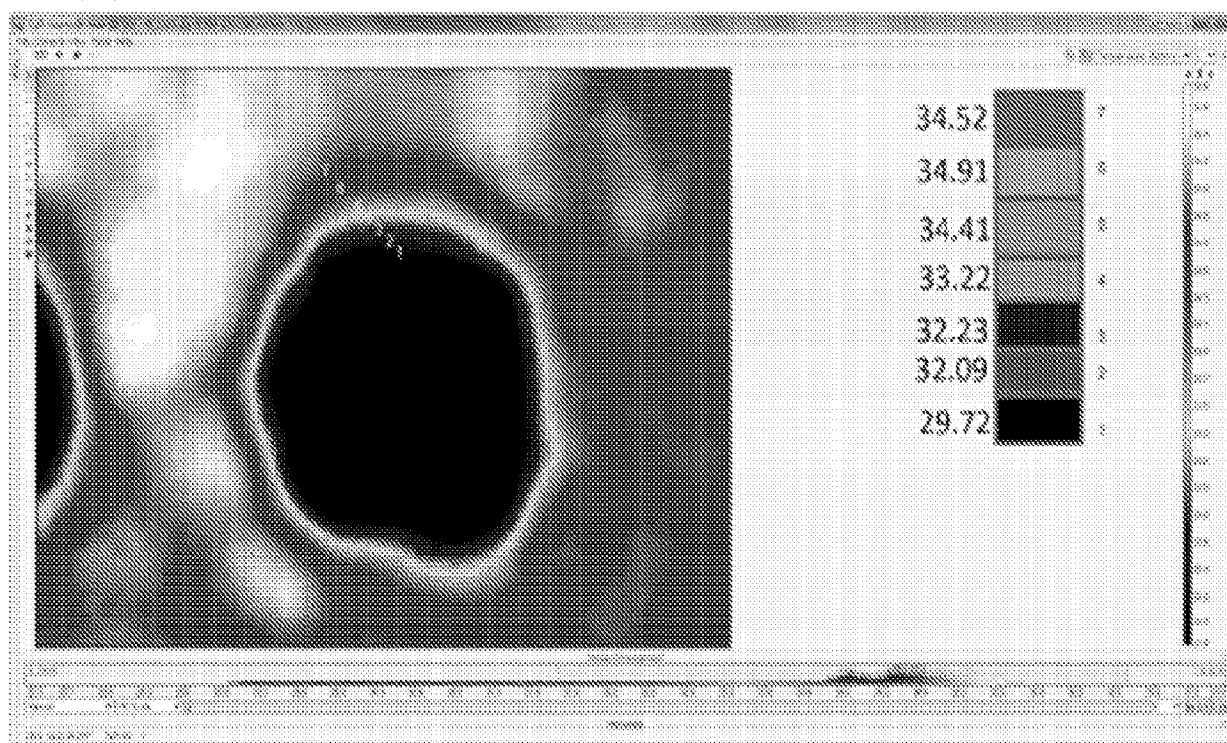
FIG 4C



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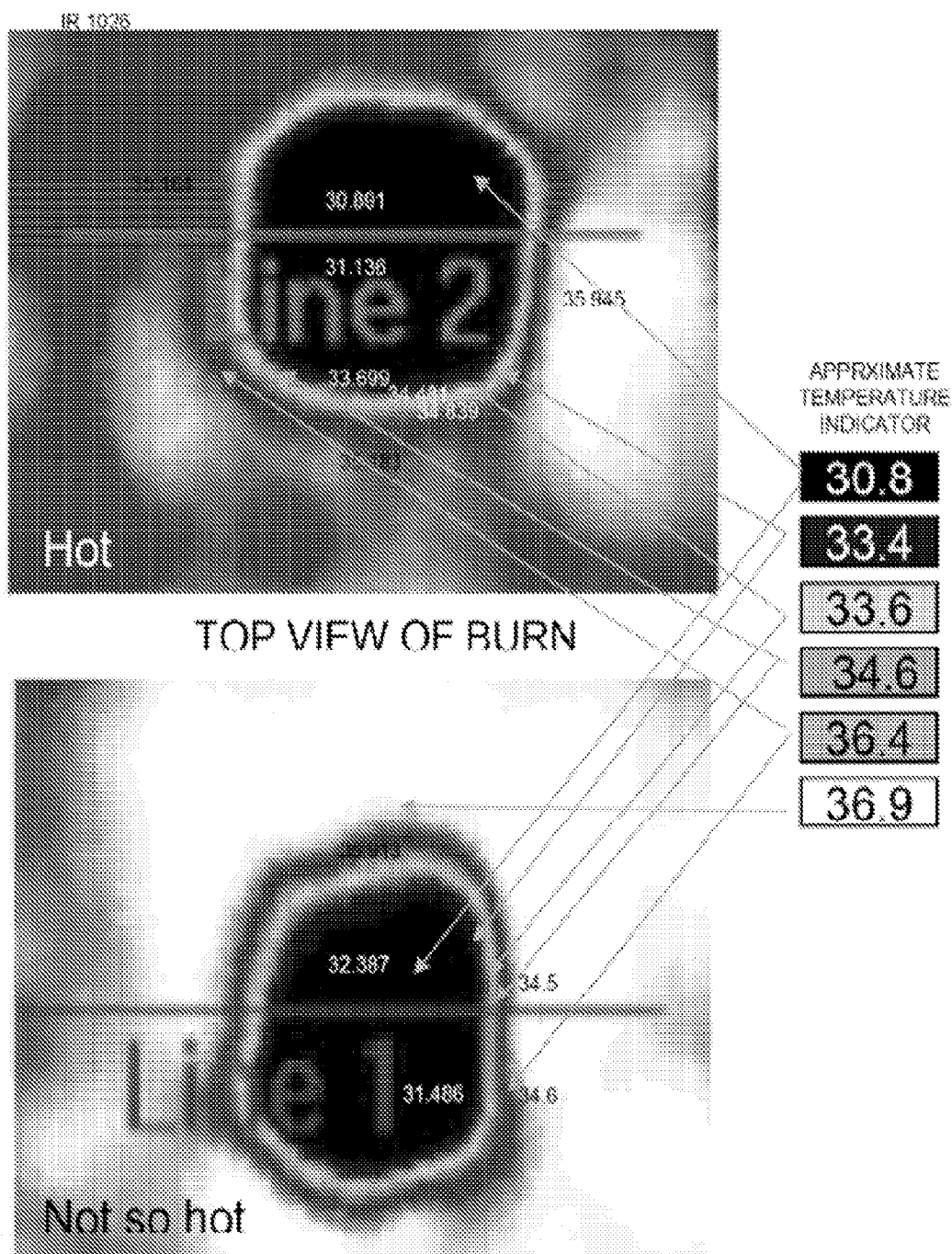
FIG 5

IR 1020



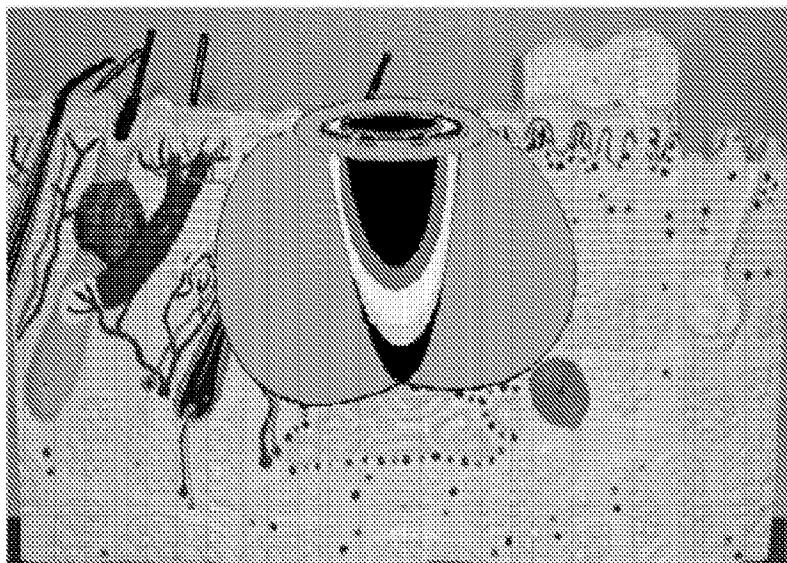
9/26

FIG 6A



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FIG 6B



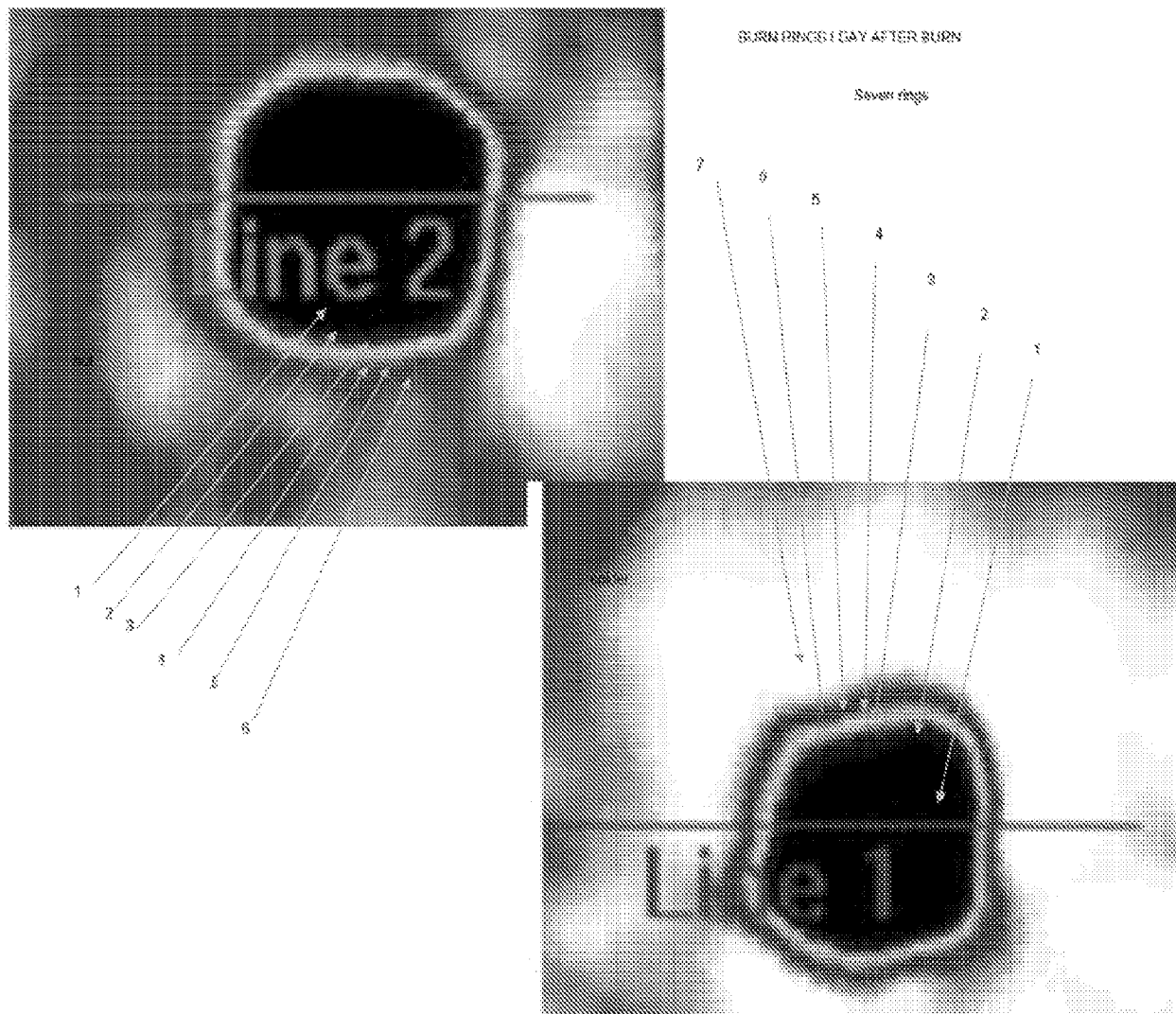
DEPTH PROFILES MODELS

FIG 6C



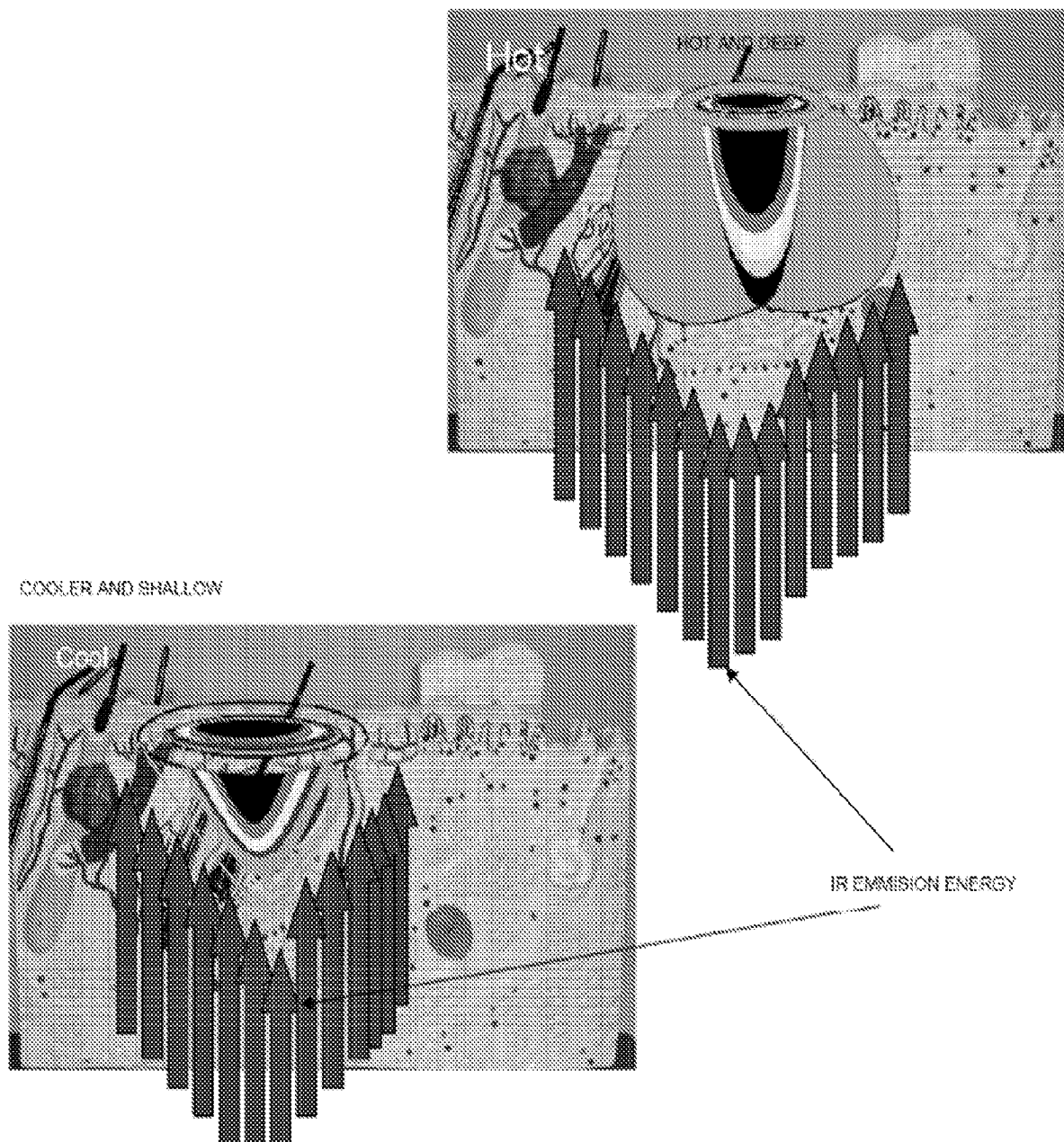
11/26

FIG 7A



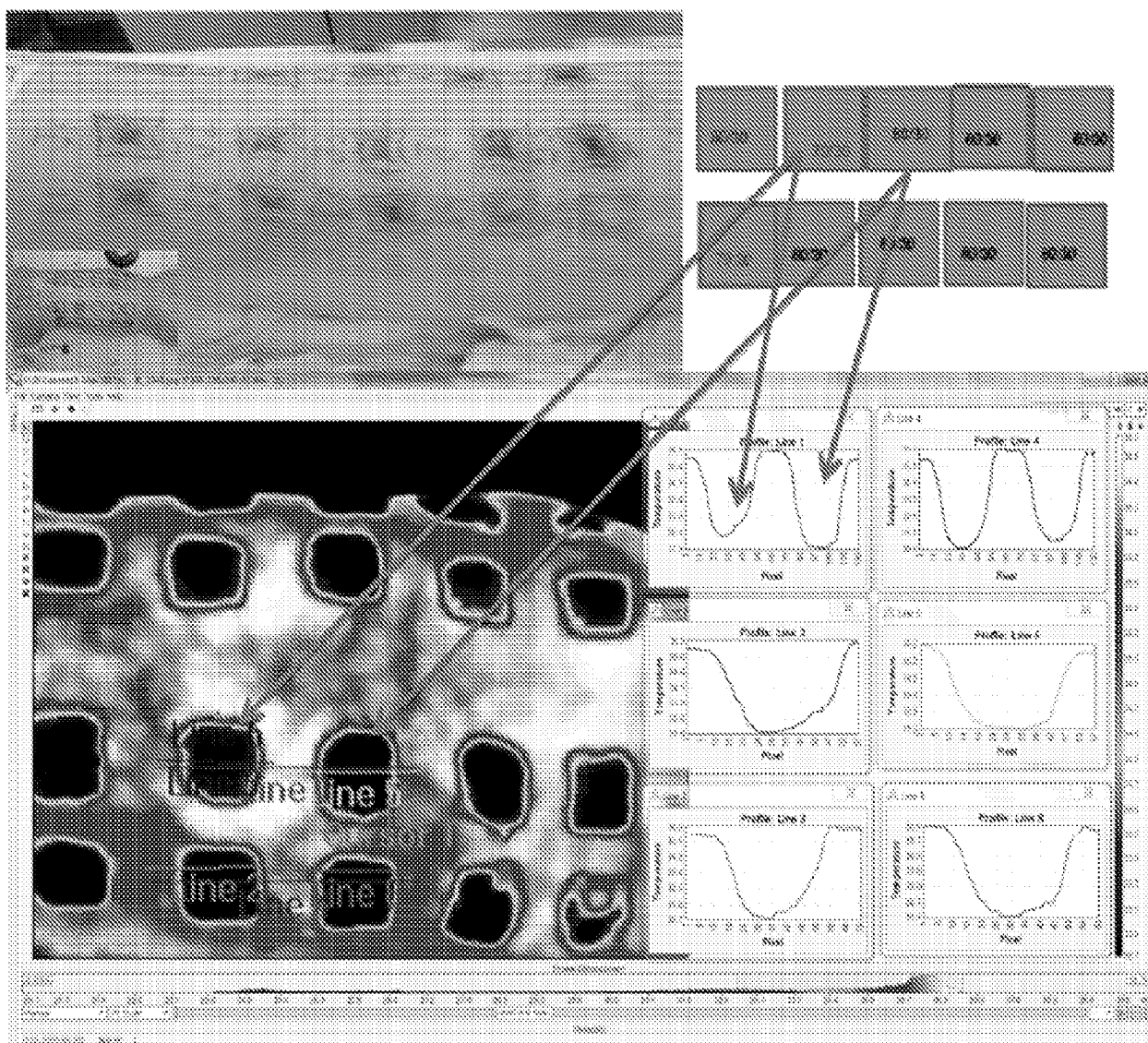
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FIG 7B



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FIG 8



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FIG 9A

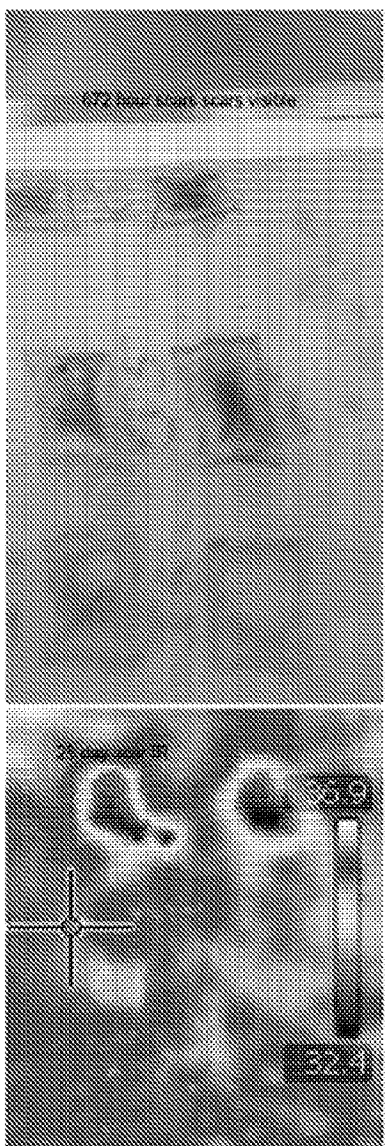
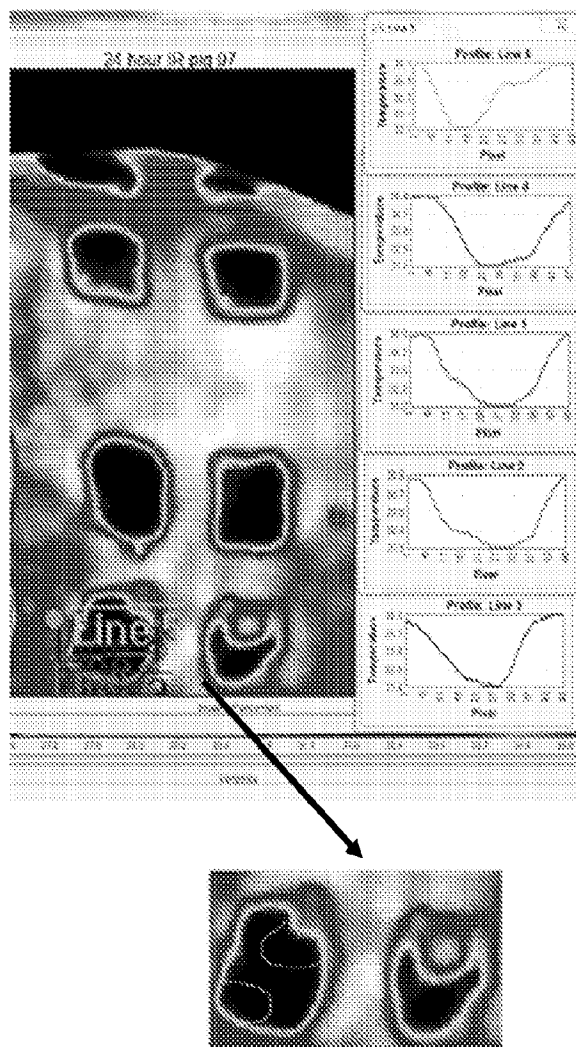
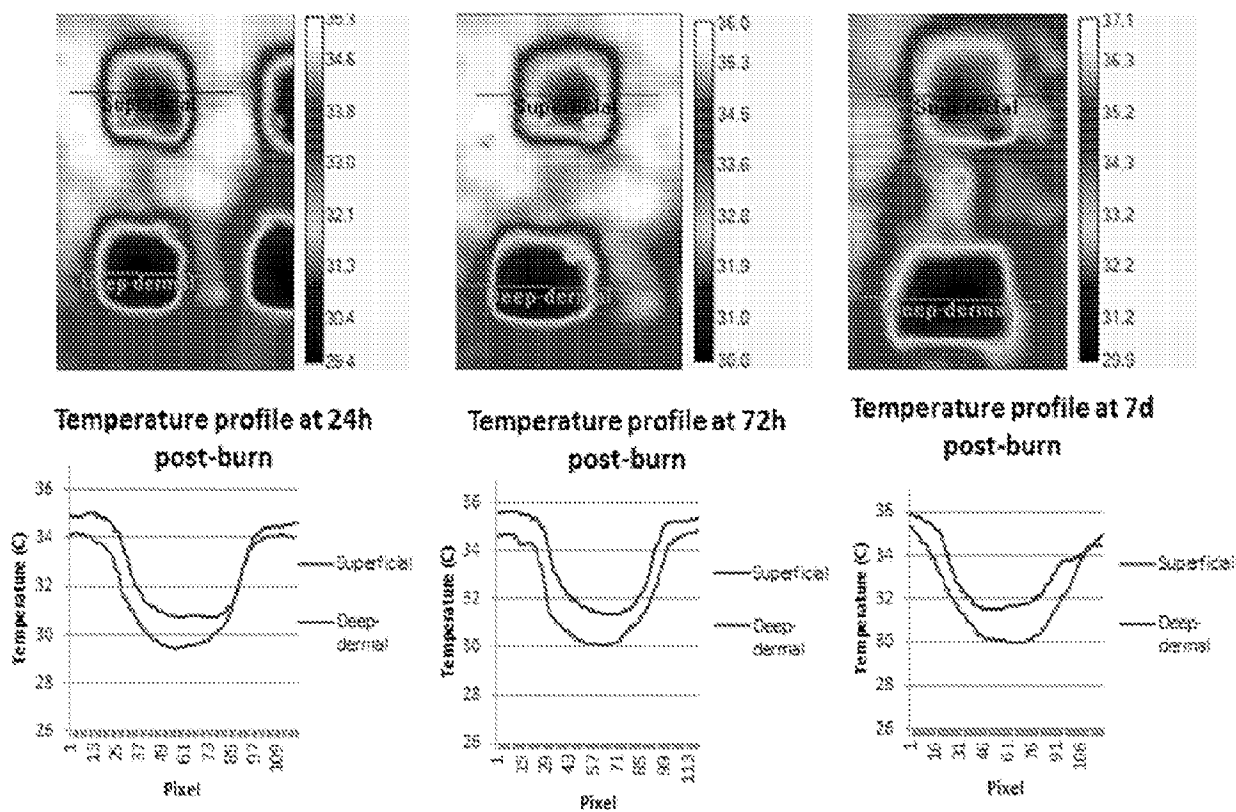


FIG 9B



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FIG 9C



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FIG 9D

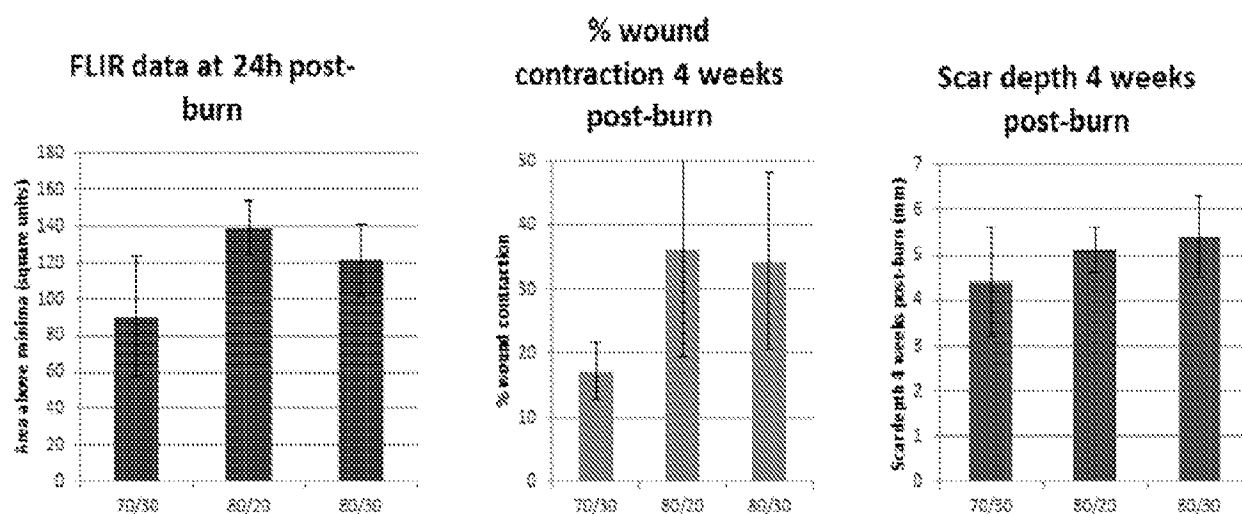
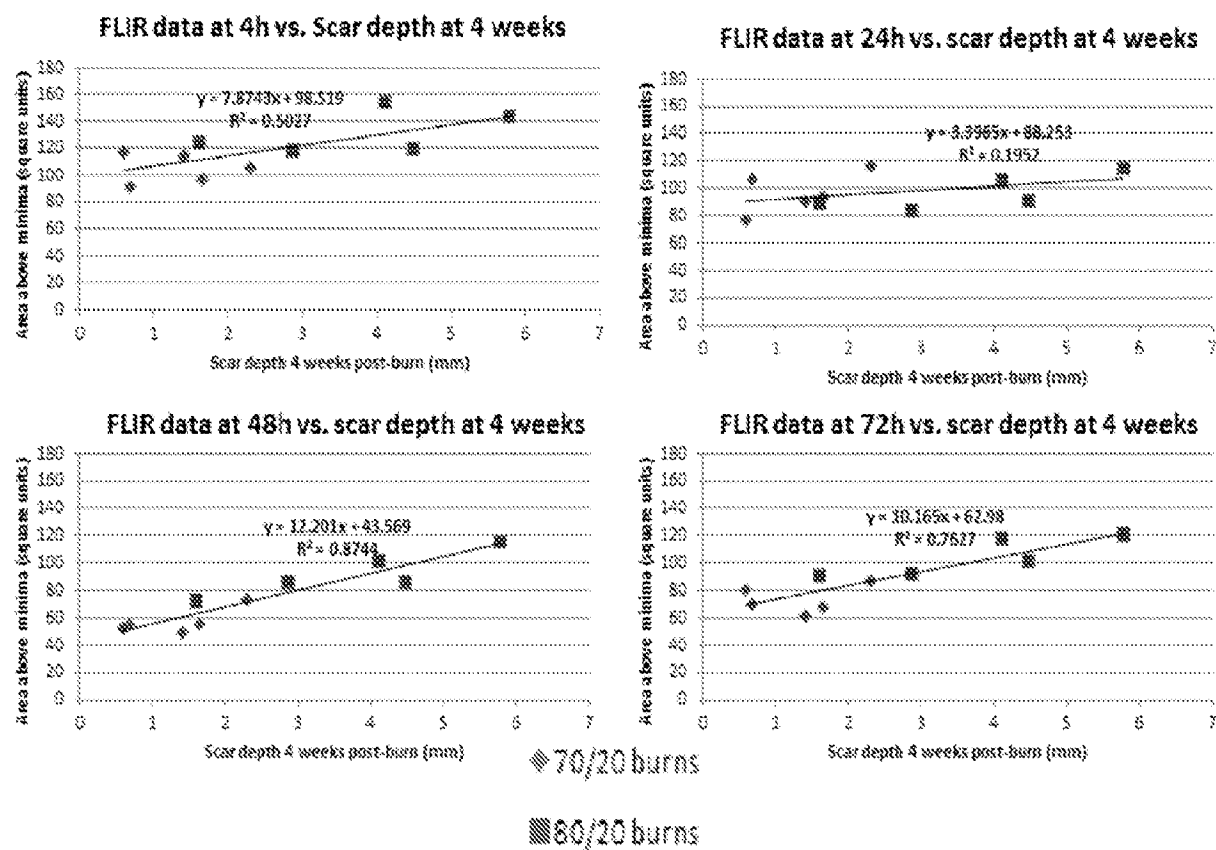
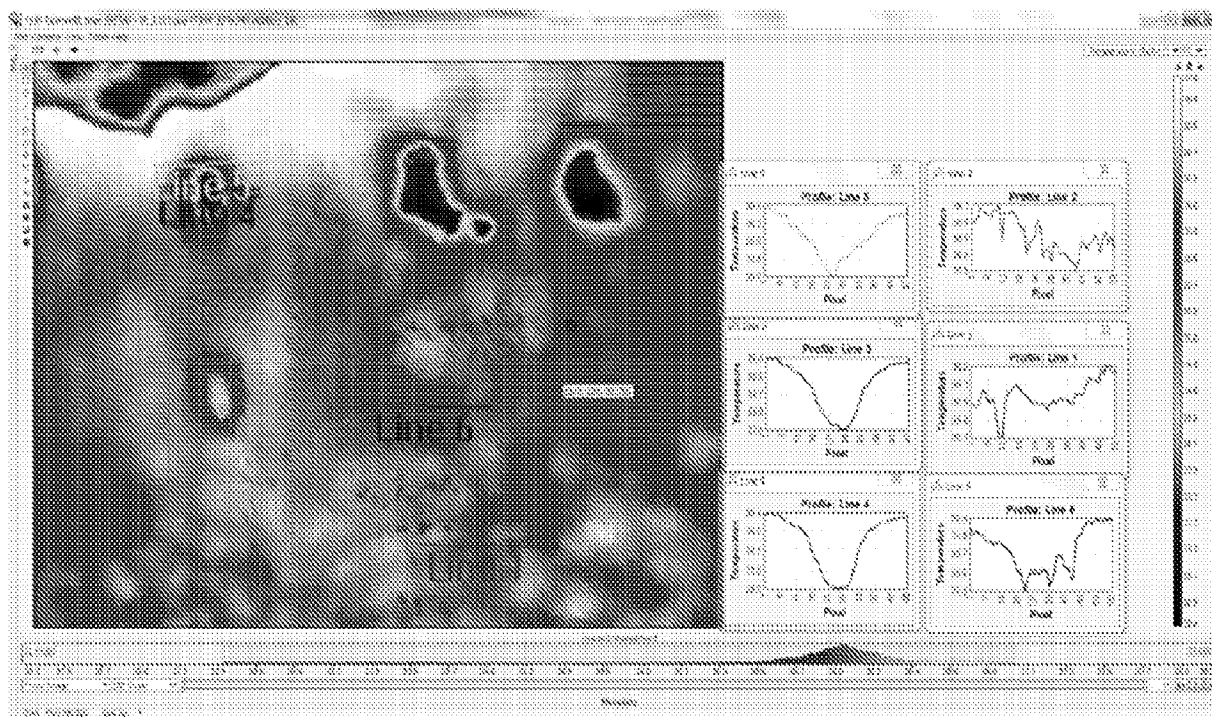


FIG 9E



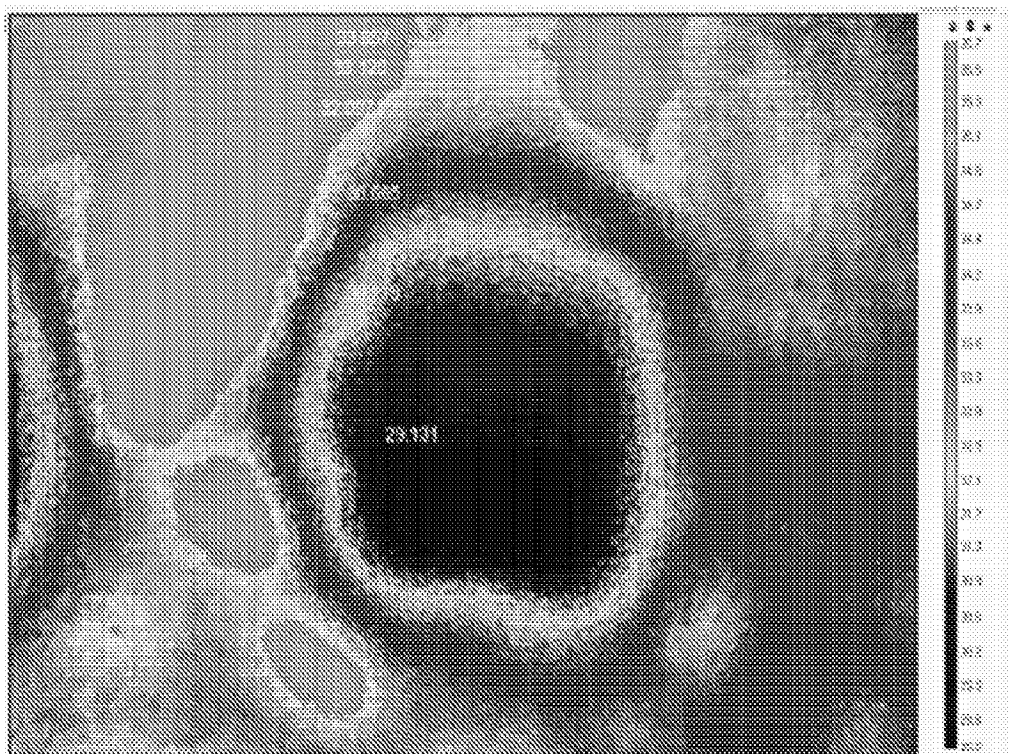
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FIG 10



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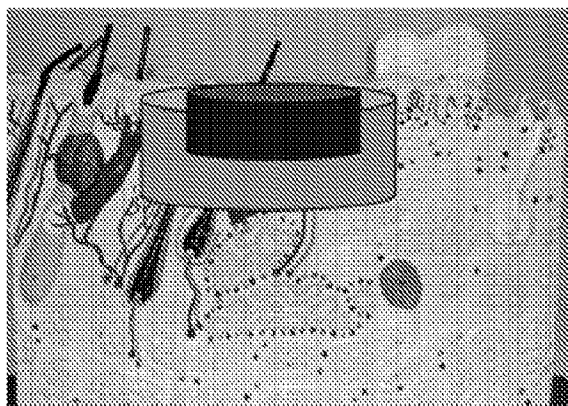
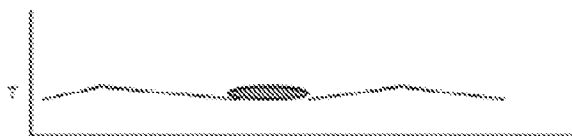
FIG 11



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FIG 12A

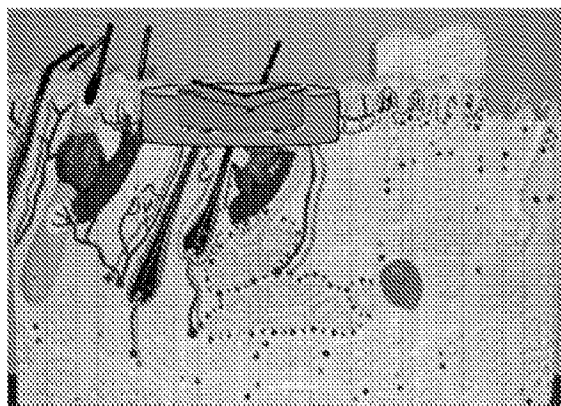
DEEP



DISTANCE FROM SPOT CENTER

FIG 12B

DEEPER QM spot exist in center but they narrow -- up as you get out from the center



DISTANCE FROM SPOT CENTER

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FIG 13A

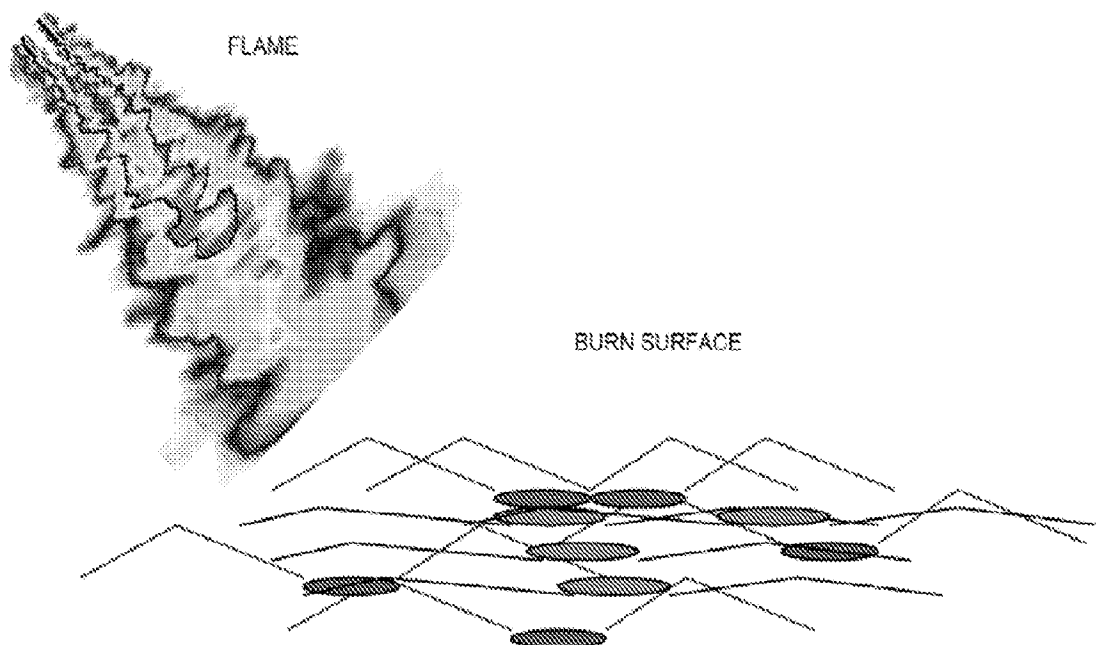


FIG 13B

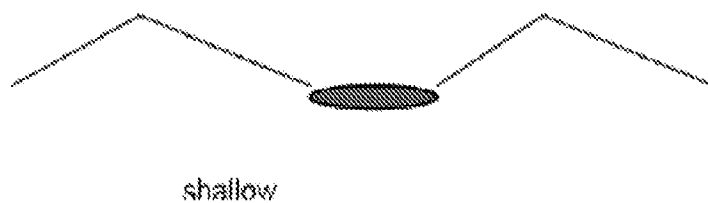
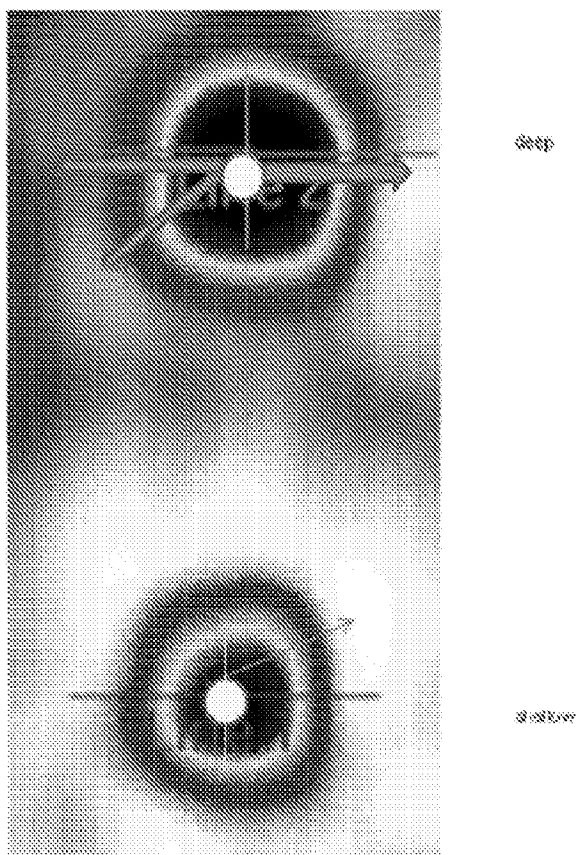


FIG 13C



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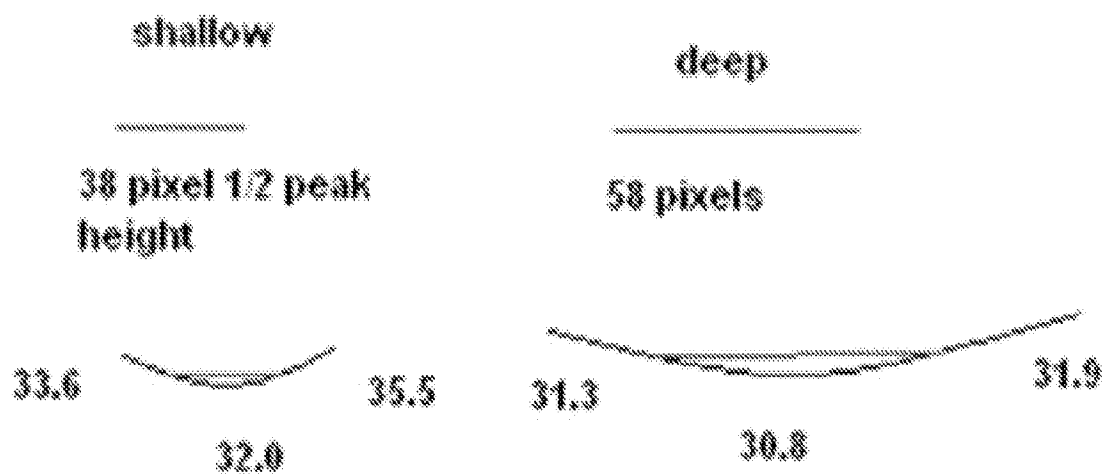
FIG 14



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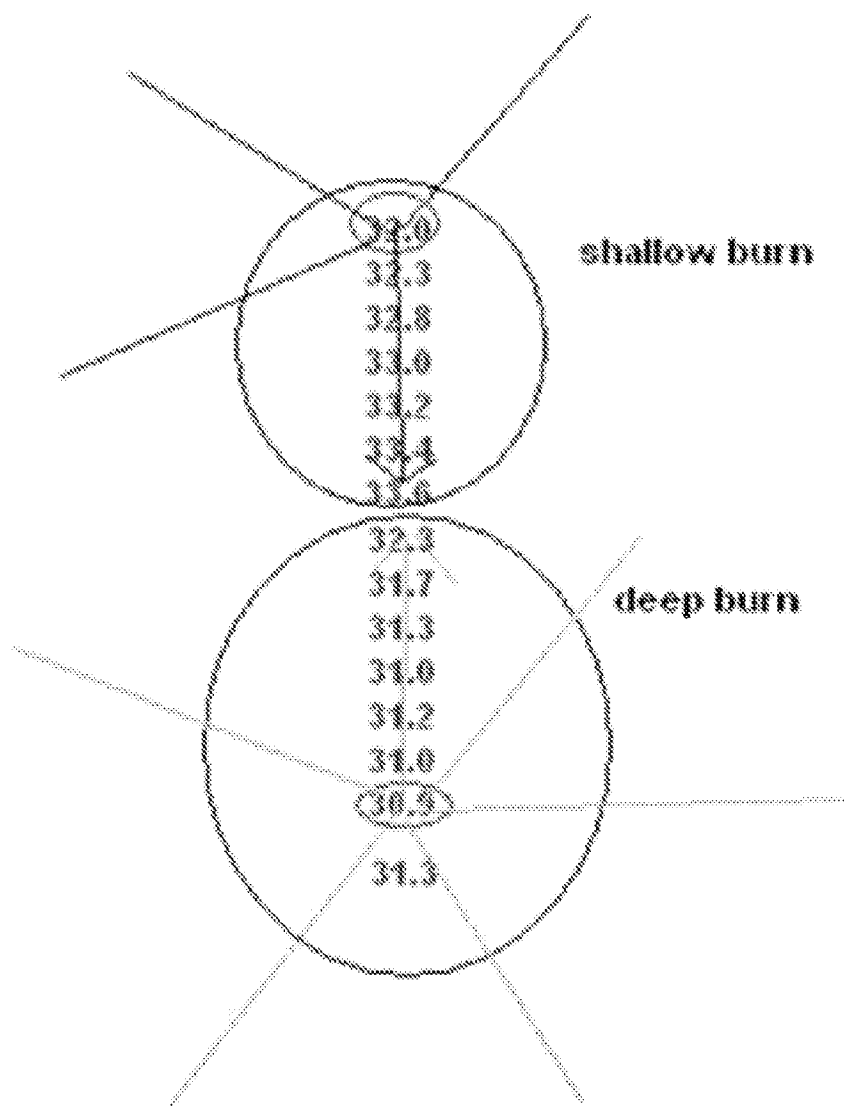
FIG 15

temperature profile across diameter of a burn



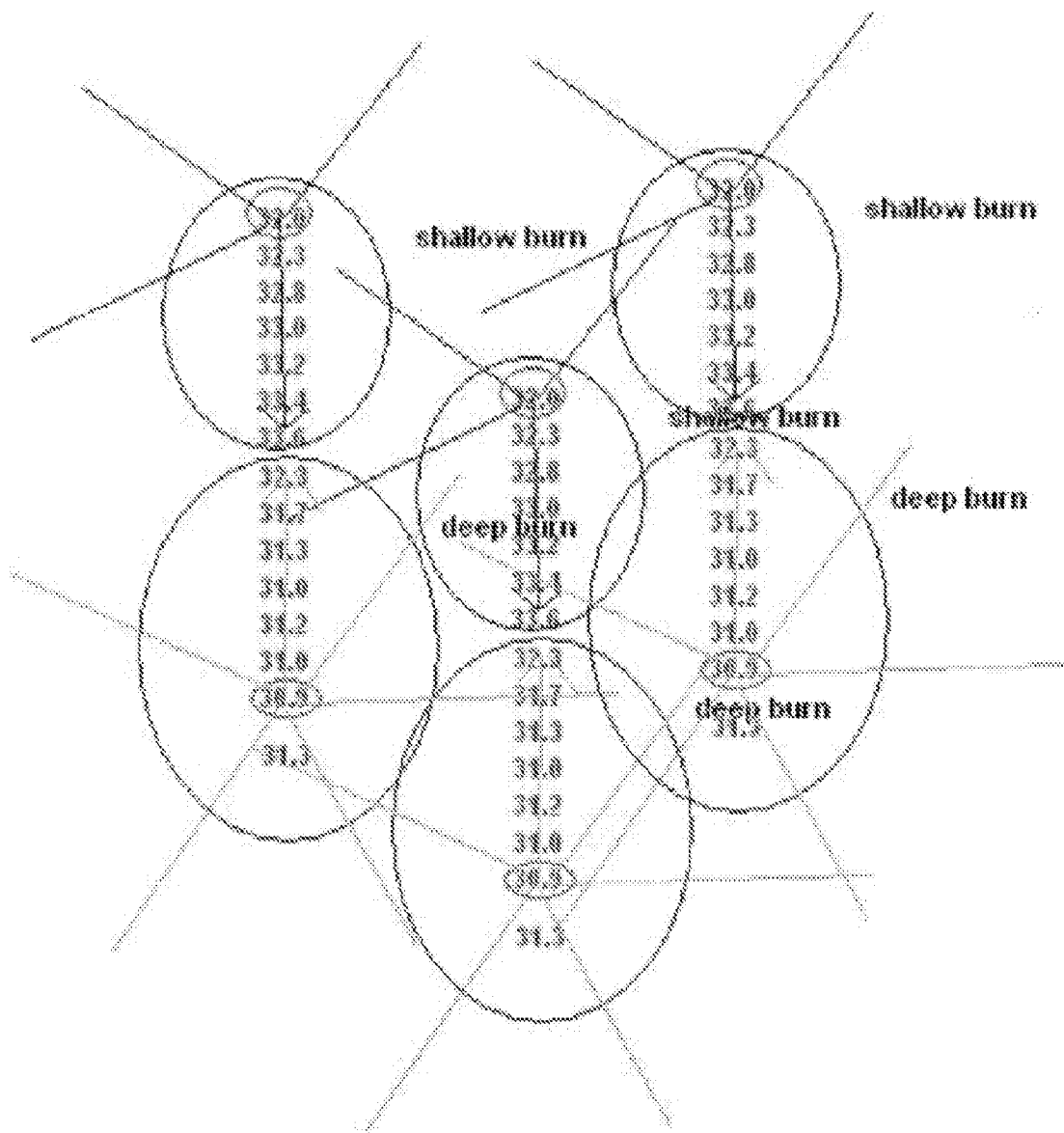
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FIG 16



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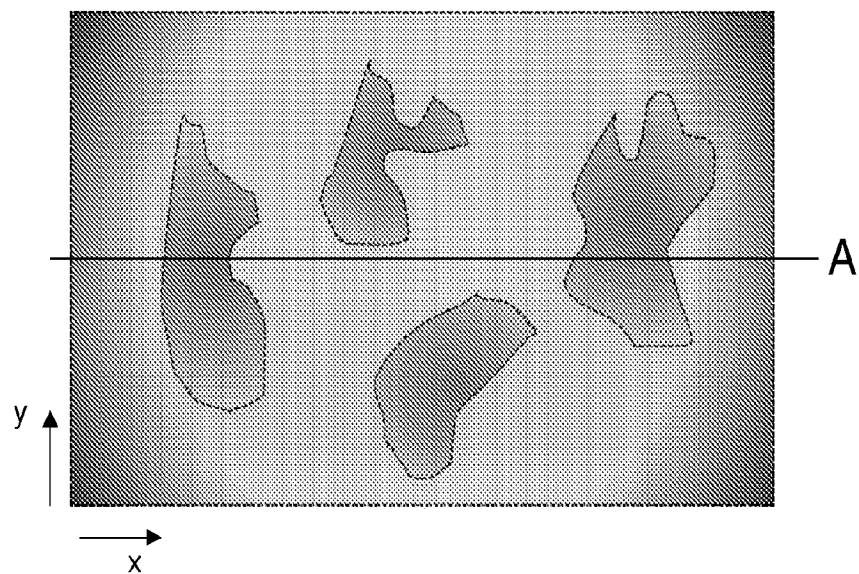
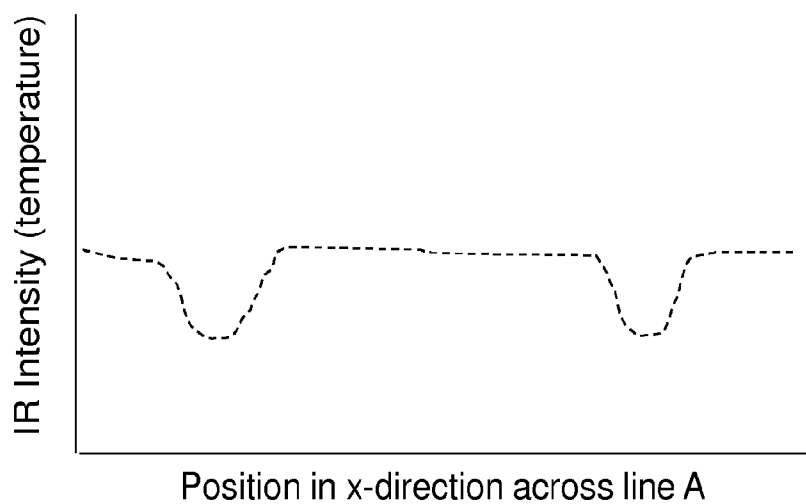
FIG 17A



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FIG 17B

IR Image of Irregular Burn Pattern



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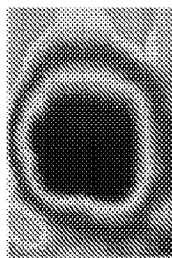


FIG 18A

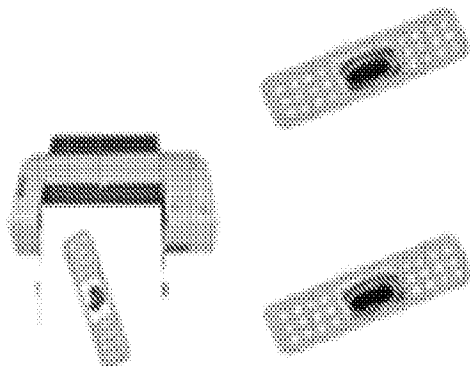


FIG 18B

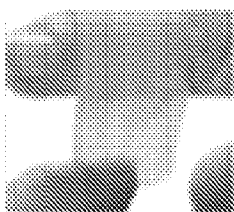


FIG 18C

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 13/22346

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61 B 5/00 (201 3.01) USPC - 600/473 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) USPC - 600/473; 600/476 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 600/473; 600/476; all classes; NPL (Keyword delimited) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Patbase (classified), Google Patents, Google Scholar Search terms used: infrared, burn, injury, wound, level, severity, pattern, emission, heat, detect#, hydration, therapeutic treatment, hours after, first, second, remove, tissue, surface, variation, density																	
C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X — Y</td> <td>US 2006/0155193 A1 (LEONARDI et al.) 13 July 2006 (13.07.2006), para [0009], [0015] [0010], [0029], [0030], [0031], [0033], [0036], [0052], [0059], [0060], 0065], [0067], [0070], [0071]; figures 4 and 5</td> <td>1-8, 15-22, 26-29 ----- 23-25, 30-38</td> </tr> <tr> <td>Y</td> <td>WO 201 1/034627 A2 (SOSTEK et al.) 24 March 201 1 (24.03.201 1), pg 26, para 1; pg 49, para 6; pg 57, para 3; pg 62, para 3; pg 82, para 5; pg 83 par 1; pg 14, para 3; claim 59</td> <td>23-25, 30-38</td> </tr> <tr> <td>X</td> <td>CA 2,287,687 A1 (HAUBENREISSER et al.) 02 May 2000 (02.05.2000); pg 12-13; claim 1, 6</td> <td>1</td> </tr> <tr> <td>A</td> <td>US 6,058,352 A (LU et al.) 02 May 2000 (02.05.2000), entire document</td> <td>1-8, 15-38</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X — Y	US 2006/0155193 A1 (LEONARDI et al.) 13 July 2006 (13.07.2006), para [0009], [0015] [0010], [0029], [0030], [0031], [0033], [0036], [0052], [0059], [0060], 0065], [0067], [0070], [0071]; figures 4 and 5	1-8, 15-22, 26-29 ----- 23-25, 30-38	Y	WO 201 1/034627 A2 (SOSTEK et al.) 24 March 201 1 (24.03.201 1), pg 26, para 1; pg 49, para 6; pg 57, para 3; pg 62, para 3; pg 82, para 5; pg 83 par 1; pg 14, para 3; claim 59	23-25, 30-38	X	CA 2,287,687 A1 (HAUBENREISSER et al.) 02 May 2000 (02.05.2000); pg 12-13; claim 1, 6	1	A	US 6,058,352 A (LU et al.) 02 May 2000 (02.05.2000), entire document	1-8, 15-38
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.															
X — Y	US 2006/0155193 A1 (LEONARDI et al.) 13 July 2006 (13.07.2006), para [0009], [0015] [0010], [0029], [0030], [0031], [0033], [0036], [0052], [0059], [0060], 0065], [0067], [0070], [0071]; figures 4 and 5	1-8, 15-22, 26-29 ----- 23-25, 30-38															
Y	WO 201 1/034627 A2 (SOSTEK et al.) 24 March 201 1 (24.03.201 1), pg 26, para 1; pg 49, para 6; pg 57, para 3; pg 62, para 3; pg 82, para 5; pg 83 par 1; pg 14, para 3; claim 59	23-25, 30-38															
X	CA 2,287,687 A1 (HAUBENREISSER et al.) 02 May 2000 (02.05.2000); pg 12-13; claim 1, 6	1															
A	US 6,058,352 A (LU et al.) 02 May 2000 (02.05.2000), entire document	1-8, 15-38															
☐ Further documents are listed in the continuation of Box C. ☐																	
<table border="0"> <tr> <td> * 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 </td> <td> "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 </td> </tr> </table>			* 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													
* 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 29 April 2013 (29.04.2013)		Date of mailing of the international search report 22 MAY 2013															
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: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774															

Form PCT/ISA/2 10 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 13/22346

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.: 9¹⁴, 39, and 45⁴⁷
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:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

- see extra 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 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.: 1-8 and 15-38

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.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 13/22346

Continuation of Box No. III - Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-8 and 15-38, drawn to a method of evaluating a burn, a wound, or a natural biological state of one or more cells, tissues, organs, organ systems, or objects, the method comprising: detecting infrared emission from a tissue burn/wound, cell, tissue, organ, system, or object; and, determining a pattern of infrared emission levels.

Group II: Claims 40-44, drawn to bandage comprising a first region having a first therapeutic compound for treating a condition, and a second region having a second therapeutic compound for treating a condition, wherein the first and second regions are configured in a pattern on the bandage that corresponds to a pattern of different levels of condition on a subject tissue.

The inventions listed as Groups I through II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I includes the special technical feature of detecting infrared emission from a tissue burn/wound, cell, tissue, organ, system, or object, not found in group II.

Group II includes the special technical feature of a bandage comprising a first region having a first therapeutic compound for treating a condition, and a second region having a second therapeutic compound for treating a condition, not found in group I.

Further,

No technical features are shared by Groups I and II that would otherwise unify the groups.

Therefore, Groups I-II lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note: Claims 9-14, 39, and 45-47 are determined to be unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a) and are, therefore, not included in any claim group.

Electronic Acknowledgement Receipt

EFS ID:	44969779
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	10-FEB-2022
Filing Date:	14-FEB-2020
Time Stamp:	17:16:53
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	067286-0410_IDSTransmittal.pdf	122225	no	3
			72b999b521592c888de5c561a80780c080078f5d		

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	067286-0410_IDS_SB08.pdf	107079	no	1
			2f0a6dcdc8cb129509de9e1184af6f5057b6907e		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Patent Term Adjustment Stmt Under 37CFR1.704(d)	067286-0410_SB133.pdf	1046201	no	2
			a79d5f9e385be024e599684d554a2ac3d3706148		
Warnings:					
Information:					
4	Foreign Reference	WO2013_110021.pdf	5269264	no	65
			d51203f237fb4dff3731d2ee22fece6bb28f1ae		
Warnings:					
Information:					
5	Non Patent Literature	JP_OA.pdf	4212572	no	13
			162b12049fa3c3fe3f8340eb7623b24b04353ce0		
Warnings:					
Information:					
6	Non Patent Literature	OA0409_012122.pdf	2824657	no	28
			eb3bb22219d2e05665d49d507b9109b953b81f45		
Warnings:					
Information:					
Total Files Size (in bytes):			13581998		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND
DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: MARLEN, TAMMIE K
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

CONCISE EXPLANATION OF RELEVANCE

Documents K1-K3 listed on the attached Form PTO/SB/08 are documents cited in a PTO Office Action of a co-pending case (serial no. 16/808,631). The relevance of the references can be found in the PTO Office Action of the co-pending case. A copy of the PTO Office Action in the co-pending case is being submitted herewith (document K5). The cited documents are in English.

Document K4 listed on the attached PTO/SB/08 is a copy of an Office Action issued in a Japanese application and English translation, dated January 11, 2022. According to an English translation of the Japanese Office Action obtained by Applicants' representative, the Japanese Patent Office made certain characterizations of the references. The disclosure of these characterizations should not be construed as an admission of or agreement to the opinions expressed in the Japanese Office Action.

STATEMENT UNDER 37 CFR §1.97(e)

For document K4, the undersigned hereby states in accordance with 37 CFR §1.97(e)(1) that each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three (3) months prior to filing of this Statement.

STATEMENT UNDER 37 CFR §1.97(e)

For documents K1-K3 and K5, the undersigned hereby states in accordance with 37 CFR §1.97(e)(2) that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of the information disclosure statement

STATEMENT UNDER 37 CFR §1.704(d)

The undersigned hereby states in accordance with 37 CFR §1.704(d) that 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 that this communication was not received by any individual designated in 37 CFR §1.56(c) more than thirty days prior to the filing of the information disclosure statement; or is a communication that was issued by a patent office in a counterpart foreign or international application or by 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.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 10, 2022

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

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 16/791,004		Filing Date 02/14/2020		☐ To be Mailed			
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO											
APPLICATION AS FILED - PART I											
		(Column 1)	(Column 2)								
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), (i), 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 \$100 =						
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 =	*		x \$460 =						
☐ 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											
		(Column 1)	(Column 2)		(Column 3)						
AMENDMENT	02/25/2022	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	* 20	Minus	** 20	= 0	x \$100 =		0			
	Independent (37 CFR 1.16(h))	* 3	Minus	*** 3	= 0	x \$480 =		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			
		(Column 1)	(Column 2)		(Column 3)						
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	*	Minus	**	=	x \$0 =					
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x \$0 =					
	☐ 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.						LIE					
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".						/DAWN BREWER/					
*** 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.											

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN

Title: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY
AND DIAGNOSIS

Appl. No.: 16/791,004

Filing Date: 2/14/2020

Examiner: Tammie K. MARLEN

Art Unit: 3792

Conf. No.: 2631

AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

This communication is responsive to the non-final Office Action dated October 25, 2021, concerning the above-referenced patent application. A payment for an extension of time is enclosed, rendering this response timely.

Amendments to the Specification begin on page 2 of this document.

Amendments to the Claims begin on page 3.

Remarks begin on page 7.

Please amend the application as follows:

Amendments to the Specification

Please amend the specification as follows:

Please replace paragraph [0001] with the following rewritten paragraph:

[0001] This application is a divisional application of U.S. Application serial number 15/292,731, filed October 13, 2016, now granted as U.S. Patent No. 10,589,122, which claims the benefit of priority to U.S. Provisional Application No. 62/241,902 filed on October 15, 2015, now expired, the entire contents of all of which are incorporated herein by reference.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A system for photodynamically diagnosing or treating a patient, comprising:
 - an illuminator comprising at least five panels connected by nested hinges on inner side surfaces of adjacent panels ~~configured to reduce optical dead space~~,
 - light sources disposed on surfaces of the at least five panels ~~a surface of the illuminator~~, the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources,
 - one of the at least five panels positioned as a center panel configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel,
 - wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges.
2. (Original) The system of claim 1, wherein the illuminator is configured to uniformly illuminate the treatment surface when the treatment surface is at a distance of two to four inches from the illuminator.
3. (Currently Amended) The system of claim 1, wherein the illuminator is configured to output red light at a dose ~~an intensity~~ of about 30 J/cm² to about 150 J/cm².
4. (Original) The system of claim 1, wherein the illuminator is configured to output light at an irradiance density of 10 mW/cm² to 30 mW/cm².
5. (Original) The system of claim 1, wherein a plurality of the light sources are configured to emit light having a wavelength in a range of 400 nm to 700 nm.

6. (Currently Amended) A method of photodynamically diagnosing or treating a patient, comprising:

administering 5-aminolevulinic acid (ALA) to the patient;

positioning an illuminator proximate to the patient, the illuminator comprising at least five panels connected by nested hinges on inner side surfaces of adjacent panels ~~configured to reduce optical dead space~~; and

uniformly illuminating a treatment surface of the patient with light sources disposed on the at least five panels of the illuminator,

wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges.

7.-10. (Cancelled).

11. (Original) The method of claim 6, further comprising determining a size of the treatment surface of the patient using a sensor.

12. (Original) The method of claim 6, further comprising determining a shape of the treatment surface of the patient using a sensor.

13. (Original) The method of claim 6, wherein at least one panel includes tabs outwardly extending from a top side and a bottom side, the tabs being configured to receive an adjacent panel therein.

14. (Original) The method of claim 11, further comprising adjusting an overall light dose with a controller based on the determined size of the treatment surface.

15. (Original) The method of claim 12, further comprising adjusting an overall light dose with a controller based on the determined shape of the treatment surface.

16. (Original) The method of claim 11, further comprising adjusting positioning of panels with at least one actuator based on the determined size of the treatment surface.

17. (Original) The method of claim 12, further comprising adjusting positioning of panels with at least one actuator based on the determined shape of the treatment surface.

18. (Currently Amended) The method of claim 6, further comprising changing intensities of the light sources of the illuminator with a controller in accordance with information received from at least one sensor relating to a curvature of the treatment surface.

19. (Currently Amended) The method of claim 6, wherein at least one panel includes a recess configured to receive a flange of [[a]] one of the nested hinges ~~hinge~~.

20. (Currently Amended) The method of claim 6,
wherein the illuminator comprises at least three first panels having first widths, at least two second panels having second widths, wherein each of the second widths of the at least two second panels is narrower than each of the first widths of the at least three first panels; and
wherein the at least three first panels and the at least two second panels are connected in an alternating ~~alternative~~ manner such that each of the at least two second panels has a first lateral side connected to a respective one of the at least three first panels and a second lateral side connected to another respective one of the at least three first panels.

21. (New) The system of claim 1, further comprising a joint provided for one of the nested hinges, the joint positioned substantially flush with an outer front surface of one panel of the at least five panels.

22. (New) The method of claim 19, wherein the recess is positioned at an inner side surface of the at least one panel.

23. (New) The system of claim 1, further comprising a recess at an inner side surface of a panel configured to accommodate a hinge joint.

24. (New) A system for photodynamically diagnosing or treating a patient, comprising:

an illuminator comprising at least five panels connected by nested hinges on inner side surfaces of adjacent panels, the nested hinges being configured so as to allow continuous illumination across the at least five panels,

light sources disposed on surfaces of the at least five panels, the illuminator being configured to uniformly illuminate a treatment surface of the patient via the light sources,

one of the at least five panels positioned as a center panel configured to face the treatment surface, and two or more of the at least five panels being configured to be angled relative to the center panel,

wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

I. Claim Status

Claims 1-20 were pending. Claims 7-10 are cancelled without prejudice or disclaimer. Claims 1, 3, 6 and 18-20 are amended. Claims 21-24 are new.

Support for the amendments to claims 1, 6, 18 and 19 may be found, e.g., in paragraphs [0009], [0027]-[0029], [0033] and [0034] of the specification as filed, in addition to Figures 2A, 2B and 8, among other portions of the original disclosure. Support for the new claims may be found, for example, in the aforementioned portions of the application as filed, in addition to paragraph [0023] and original claim 1. For example, Figure 8 (with associated text in paragraph [0034]) shows continuous illumination. The amendments, including the above-noted cancellation of claims 7-10, are made without acquiescing to the propriety of any objection or rejection and without introducing new matter.

II. Record of Interview Substance

Applicant sincerely appreciates the courtesy of the videoconference interview between Primary Examiner Marlen and the undersigned representatives on January 24, 2022. The PTO-issued interview summary dated January 27, 2022 generally summarizes the topics discussed during the interview, although Applicant does not acquiesce to the propriety of all of the characterizations of the proposed amendments in regard to potential further rejections under section § 112(b). Applicant thanks Primary Examiner Marlen for the indication that the proposed amendments would overcome the prior rejections under §§ 102, 103 and 112(b), and for her time and suggestions.

III. Information Disclosure Statements

Applicant appreciates the consideration given to the Information Disclosure Statements (IDSs) filed prior to issuance of the pending Office Action. Applicant respectfully requests consideration given to the IDSs filed on November 18, 2021, December 20, 2021 and February

10, 2022 (after the issuance of the current Office Action) and that signed PTO/SB/08 forms be provided in the next communication to Applicant's representatives.

IV. Objection to the Specification

The specification was objected to for not containing current status information of applications identified in the cross-reference to related applications in paragraph [0001] of the specification. The specification is revised as indicated.

V. Claim Rejection under 35 U.S.C. § 112

Claims 1-20 were rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph, as allegedly being indefinite. For at least the following reasons, this rejection should be withdrawn.

Without conceding to the propriety of the rejection, claims 7-10 are cancelled to expedite prosecution and the remaining claims are amended to address each point raised in the rejection, in a manner believed to resolve the concerns stated in the Office Action. Applicant therefore respectfully requests favorable reconsideration and withdrawal of the rejection.

VI. Claim Rejections under 35 U.S.C. § 102

Claims 1, 2, 6, 7, 13, 18 and 19 were rejected under 35 U.S.C. § 102(a)(1) as allegedly anticipated by U.S. Patent Publication No. 2007/0283655 ("Tobin"). Claims 1, 2, 5-7 and 18 were rejected under 35 U.S.C. § 102(a)(1) as allegedly anticipated by U.S. Patent Publication No. 2005/0075703 ("Larsen"). For at least the following reasons, the rejections should be withdrawn.

Neither Tobin nor Larsen discloses or teaches a system or a method involving an illuminator "wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges," as recited in claims 1 and 6, as amended. Tobin discloses an illuminator including panels of different sizes, as seen in Figure 2, and Larsen discloses an illuminator with tubular light sources, as seen in Figure 17b. Neither Tobin or Larsen discloses or teaches an illuminator with light sources arranged so as to provide a higher intensity of light

emitted proximate second edges of the panels, which are shorter than first edges of the panels, as compared to the intensity of light emitted not proximate the second edges.

For at least these reasons, claims 1 and 6 are allowable over Larsen and Tobin. Claims 2, 5-7, 13, 18 and 19 are allowable therewith, without regard to their further patentable recitations. Applicant respectfully solicits favorable consideration and withdrawal of the rejections.

VII. Claim Rejections under 35 U.S.C. § 103

Claims 3-5 were rejected under 35 U.S.C. § 103 as allegedly unpatentable over Tobin in view of U.S. Patent Publication No. 2003/0216795 (“Harth”). Claims 11, 12 and 14-17 were rejected under 35 U.S.C. § 103 as allegedly unpatentable over Tobin in view of U.S. Patent Publication No. 2013/0066404 (“Tapper”). Claims 3 and 4 were rejected under 35 U.S.C. § 103 as allegedly unpatentable over Larsen in view of Harth. Claims 11, 12 and 14-17 were rejected under 35 U.S.C. § 103 as allegedly unpatentable over Larsen in view of Tapper. Claim 20 was rejected under 35 U.S.C. § 103 as allegedly unpatentable over Larsen. For at least the following reasons, the rejections should be withdrawn.

As discussed above, neither Tobin nor Larsen discloses or teaches a system or a method including all the features of claims 1 and 6 as amended. Neither Harth nor Tapper cures the defects of either Tobin or Larsen. Hence, claims 3-5, 11, 12, 14-17 and 20 are allowable by virtue of their dependence from claim 1 or claim 6, as amended, without regard to their further patentable recitations. Favorable reconsideration and withdrawal of the rejections are respectfully requested.

VIII. Conclusion

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application is respectfully requested.

Primary Examiner Marlen is invited to contact the undersigned to advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to

Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extension fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date: 25 Feb 2022

FOLEY & LARDNER LLP
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By /Kiri Lee Sharon/

Glenn Law
Attorney for Applicant
Registration No. 34,371

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828

Electronic Patent Application Fee Transmittal

Application Number:	16791004			
Filing Date:	14-Feb-2020			
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS			
First Named Inventor/Applicant Name:	Thomas Boyajian			
Filer:	Kiri Lee Sharon/Effie Hale			
Attorney Docket Number:	067286-0410			
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(\$)
Extension - 1 month with \$0 paid	1251	1	220	220
Miscellaneous:				
Total in USD (\$)				220

Electronic Acknowledgement Receipt

EFS ID:	45092132
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Kiri Lee Sharon/Effie Hale
Filer Authorized By:	Kiri Lee Sharon
Attorney Docket Number:	067286-0410
Receipt Date:	25-FEB-2022
Filing Date:	14-FEB-2020
Time Stamp:	17:16:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$ 220
RAM confirmation Number	E202220H17552316
Deposit Account	190741
Authorized User	Effie Hale

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:
37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		ResponseNFOA.pdf	163526	yes	10
			6cc8603aaad3d996c1c1bfbdd6acb702cc974fd38		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Amendment/Request for Reconsideration-After Non-Final Rejection		1	1	
	Specification		2	2	
	Claims		3	6	
	Applicant Arguments/Remarks Made in an Amendment		7	10	
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	38536	no	2
			41d01d45fe784ab2db266ad9acaa04f7c0b8544c		
Warnings:					
Information:					
Total Files Size (in bytes):			202062		

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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.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 4, 2022 <i>(use as many sheets as necessary)</i>			Complete if Known	
			Application Number	16/791,004
			Filing Date	2/14/2020
			First Named Inventor	Thomas BOYAJIAN
			Art Unit	3792
Examiner Name	MARLEN, TAMMIE K			
Attorney Docket Number	067286-0410			
Sheet	1	of	1	

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	L1	MAISCH ET AL., Fluorescence Induction of Protoporphyrin IX by a New 5-Aminolevulinic Acid Nanoemulsion Used for Photodynamic Therapy in a Full-Thickness ex vivo Skin Model, Experimental Dermatology, 19, 2009, pp. e302-e305	
	L2	NUCCI ET AL., Treatment of Anogenital Condylomata Acuminata with Topical Photodynamic Therapy: Report of 14 Cases and Review, International Journal of Infectious Diseases, 14S, 2010, pp. e280-e282	
	L3	USPTO Non-Final Office Action, 16/631,205 (067286-0423), 03/03/2022, 31 pages	
	L4	WILLEY ET AL., American Society for Laser Medicine and Surgery Abstracts, #147, Ultra Fast Thermal PDT for Facial AKs: Proof of Concept Study, March 2017, 2 pages	

Examiner Signature		Date Considered	
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Electronic Acknowledgement Receipt

EFS ID:	45391027
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	04-APR-2022
Filing Date:	14-FEB-2020
Time Stamp:	17:03:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	067286-0410_IDS_Transmittal.pdf	120657 023d7f355da72d520cb19799d3dbda52b7bd3c98	no	3

Warnings:

Information:					
2	Patent Term Adjustment Statement under 37 CFR 1.704(d) filed with an IDS	067286-0410_SB0133.pdf	1046711	no	2
			32768fa2c2a7b8a662bdde6569a1f89fab1952a9		
Warnings:					
Information:					
3	Non Patent Literature	MAISCH.pdf	597075	no	4
			5763a92ccbfcd7c0fdbb3a9412f531464f8dfdfc		
Warnings:					
Information:					
4	Non Patent Literature	NUCCI_.pdf	478131	no	3
			d070b688ebc9025c9e5c89e54bf48bc10dfbca62		
Warnings:					
Information:					
5	Non Patent Literature	OA_0423_0322.pdf	3020585	no	31
			046d0e87b218297eb05c810ccb80aaba98eca9d6		
Warnings:					
Information:					
6	Non Patent Literature	WILLEYetal.pdf	343603	no	2
			55a83c3e9a3c5007ebf23cbd356a60f83cea96dd		
Warnings:					
Information:					
7	Information Disclosure Statement (IDS) Form (SB08)	067286-0410_IDS_SB08.pdf	108116	no	1
			4b62f2863d5edf824c6643be9fb86a1c4b7cad33		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
Total Files Size (in bytes):			5714878		

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR
FOR PHOTODYNAMIC
THERAPY AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: MARLEN, TAMMIE K
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith a document for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that the listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action, which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed document is being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

CONCISE EXPLANATION OF RELEVANCE

A PTO Office Action and references issued in a co-pending case (serial no. 16/631,205) are being submitted.

However, in accordance with MPEP § 609.04(a)(I), for the Maisch and Nucci documents, Applicant hereby states that the date of publication supplied does not include the month of publication, however the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue.

STATEMENT UNDER 37 CFR §1.97(e)

The undersigned hereby states in accordance with 37 CFR §1.97(e)(2) that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of the information disclosure statement.

STATEMENT UNDER 37 CFR §1.704(d)

The undersigned hereby states in accordance with 37 CFR §1.704(d) that 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 that this communication was not received by any individual designated in 37 CFR §1.56(c) more than thirty days prior to the filing of the information disclosure statement; or is a communication that was issued by a patent office in a counterpart foreign or international application or by 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.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date April 4, 2022

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371

PATENT TERM ADJUSTMENT STATEMENT UNDER 37 CFR 1.704(d)

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3792
Examiner Name	MARLEN, TAMMIE K
Practitioner Docket No.	067286-0410

APPLICANT HEREBY STATES THE FOLLOWING (please review 37 CFR 1.704(d) before filing this form):

☒ 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 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

AND/OR

☒ Each item of information contained in the information disclosure statement is a communication that was issued by a patent office in a counterpart foreign or international application or by the Office, and this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

INSTRUCTIONS:

- **This form will not satisfy the requirement of 37 CFR 1.97(e).** The present statement is filed under 37 CFR 1.704(d) and will not substitute for compliance with any of the requirements of 37 CFR 1.97 and 1.98. For an information disclosure statement to comply with 37 CFR 1.97(c) or (d), the information disclosure statement must be accompanied by a statement under 37 CFR 1.97(e) notwithstanding any statement filed under 37 CFR 1.704(d).
- The present form (PTO/SB/133) should be filed concurrently with the information disclosure statement to derive benefit under 37 CFR 1.704(d).

Signature	/Glenn Law/	Date	4/4/2022
Typed or Printed Name	Glenn Law	Practitioner Registration Number	34,371
<p>Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.</p>			
☒	*Total of <u>1</u> forms are submitted.		

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Substitute for form 1449/PTO
**INFORMATION DISCLOSURE
 STATEMENT BY APPLICANT**

Date Submitted: May 3, 2022

(use as many sheets as necessary)

Complete if Known

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3792
Examiner Name	MARLEN, TAMMIE K
Attorney Docket Number	067286-0410

Sheet 1 of 1

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)			
	M1	8,226,289-B2	07-24-2012	LINDEBERG	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	M2	Australian Examination Report, Application No. 2020267186, 2/3/2022, 4 pages	
	M3	Australian Examination Report, Application No. 2021107564, 4/4/2022, 4 pages	
	M4	Notice of Allowance, 17/487,698 (067286-0437), 04/29/2022, 11 pages	

Examiner
Signature

Date
Considered

Electronic Acknowledgement Receipt

EFS ID:	45625032
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Glenn Law/Effie Hale
Filer Authorized By:	Glenn Law
Attorney Docket Number:	067286-0410
Receipt Date:	03-MAY-2022
Filing Date:	14-FEB-2020
Time Stamp:	16:30:40
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	067286-0410_IDS_Transmittal.pdf	119504 7d6a2c79ddd1eed4394a192749d22940d1351713	no	3

Warnings:

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	067286-0410_IDS_SB08.pdf	106720	no	1
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
3	Non Patent Literature	AUExamRpt_020322.pdf	1810982	no	4
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Information:					
4	Non Patent Literature	AUExamRpt_040422.pdf	1122660	no	4
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Warnings:					
Information:					
Total Files Size (in bytes):			4293371		
<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>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN

Title: ADJUSTABLE
ILLUMINATOR FOR
PHOTODYNAMIC THERAPY
AND DIAGNOSIS

Application No.: 16/791,004

Filing Date: 2/14/2020

Examiner: MARLEN, TAMMIE K

Art Unit: 3792

Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action, which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(c), before the mailing date of any of a final action under 37 CFR §1.113, a notice of allowance under 37 CFR §1.311, or an action that otherwise closes prosecution in the application.

CONCISE EXPLANATION OF RELEVANCE

Documents M2 and M3 listed on the attached PTO/SB/08 are copies of Examination Reports issued in Australian applications dated February 3, 2022 and April 4, 2022, respectively.

Document M1 listed on the attached Form PTO/SB/08 is a document cited in a PTO Notice of Allowance issued in a co-pending case (serial no. 17/487,698). A copy of the Notice of Allowance is being submitted herewith (document M4).

STATEMENT UNDER 37 CFR §1.97(e)

For documents M1 and M4, the undersigned hereby states in accordance with 37 CFR §1.97(e)(2) that no item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR §1.56(c) more than three months prior to the filing of the information disclosure statement.

STATEMENT UNDER 37 CFR §1.97(e)

For documents M2 and M3, the undersigned hereby states in accordance with 37 CFR §1.97(e)(1) that each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three (3) months prior to filing of this Statement.

Although Applicant believes that no fee is required, the Commissioner is hereby authorized to charge any additional fees which may be due to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 3, 2022

By /Glenn Law/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5426
Facsimile: (202) 672-5399

Glenn Law
Attorney for Applicant
Registration No. 34,371



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

NOTICE OF ALLOWANCE AND FEE(S) DUE

22428 7590 05/16/2022
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

EXAMINER

MARLEN, TAMMIE K

ART UNIT

PAPER NUMBER

3792

DATE MAILED: 05/16/2022

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631

TITLE OF INVENTION: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	08/16/2022

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

22428 7590 05/16/2022
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631

TITLE OF INVENTION: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	08/16/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
MARLEN, TAMMIE K	3792	607-090000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

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.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	05/16/2022	EXAMINER	
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	

DATE MAILED: 05/16/2022

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. 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 30 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, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. 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.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/791,004	Applicant(s) Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment filed on 2/25/2022.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ 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.

3. ☒ The allowed claim(s) is/are 1-6 and 11-24. As a result of the allowed claim(s), 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.

4. ☐ 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)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)	5. ☐ Examiner's Amendment/Comment
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.	6. ☒ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.	7. ☐ Other _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.	

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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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.

Information Disclosure Statement

2. Applicant should note that the large number of references in the attached IDS have been considered by the examiner in the same manner as other documents in Office search files are considered by the examiner while conducting a search of the prior art in a proper field of search. **See MPEP 609.05(b).** Applicant is requested to point out any particular references in the IDS which they believe may be of particular relevance to the instant claimed invention in response to this office action.

Allowable Subject Matter

3. Claims 1-6 and 11-24 are allowed.

4. The following is an examiner's statement of reasons for allowance: It is in the opinion of the examiner that the art of record neither anticipates nor renders obvious "nested hinges on inner side surfaces of adjacent panels" and "wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges" in combination with the rest of the claimed limitations set forth in the independent claim.

Searching by the Examiner yielded prior art as cited in the previous Office Actions. Based on Applicant's arguments and the Examiner's review of the Office Action mailed on October 25, 2021, the subject matter is deemed to be allowable. Further explanation can be reviewed in the Applicant's arguments filed on February 25, 2022. Therefore, it is concluded by the examiner that claims 1-6 and 11-24 of the present invention are allowable..

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMMIE K MARLEN whose telephone number is (571)272-1986. The examiner can normally be reached Monday through Friday from 8 am until 4 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on 571-272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TAMMIE K MARLEN/
Primary Examiner, Art Unit 3792

Search Notes 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

CPC - Searched*		
Symbol	Date	Examiner
A61N 5/06,062,0616	10/20/2021	TKM
A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662	10/20/2021	TKM
A61B5/0064,0082	10/20/2021	TKM
Updated above	05/06/2022	TKM

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name and assignee search	10/20/2021	TKM
Text-limited and related application search – see search history printout	10/20/2021	TKM
Consulted Alyssa Alter	10/20/2021	TKM
Updated above	05/06/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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<i>Search Notes</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	PGPUB text search -- see interference search printout	05/06/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	

CPC						
Symbol					Type	Version
A61N	/	5	/	062	F	2013-01-01
A61B	/	5	/	0064	I	2013-01-01
A61B	/	5	/	0082	I	2013-01-01
A61N	/	2005	/	0633	A	2013-01-01
A61N	/	2005	/	0626	A	2013-01-01
A61N	/	2005	/	0642	A	2013-01-01
A61N	/	2005	/	0652	A	2013-01-01
A61N	/	2005	/	0663	A	2013-01-01
A61N	/	2005	/	0662	A	2013-01-01
A61N	/	2005	/	0651	A	2013-01-01

CPC Combination Sets					
Symbol				Type	Set
	/		/		

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) _____		06 May 2022 (Date)	O.G. Print Claim(s) 1 O.G. Print Figure 2A

Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61N5/06	/	5	/ 06
NON-CLAIMED			
/	/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	06 May 2022	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	2A

Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1		10	17	19										
2	2	9	11	19	20										
3	3	12	12	6	21										
4	4	15	13	18	22										
5	5	10	14	7	23										
8	6	13	15	20	24										
	7	11	16												
	8	14	17												
	9	16	18												

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) 06 May 2022		O.G. Print Claim(s) 1	O.G. Print Figure 2A

Bibliographic Data

Application No: 16/791,004

Foreign Priority claimed: ☐ Yes ☒ No

35 USC 119 (a-d) conditions met: ☐ Yes ☒ No ☐ Met After Allowance

Verified and Acknowledged: /TAMMIE K MARLEN/

Examiner's Signature

Initials

Title:

ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC
THERAPY AND DIAGNOSIS

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
02/14/2020	607	3792	067286-0410
RULE			

APPLICANTS

DUSA Pharmaceuticals, Inc., Wilmington, MA,

INVENTORS

Thomas Boyajian, Wilmington, MA, UNITED STATES

Mark Carota, Chelmsford, MA, UNITED STATES

Brian Mazejka, Salem, NH, UNITED STATES

CONTINUING DATA

This application is a DIV of 15292731 10/13/2016 PAT 10589122

15292731 has PRO of 62241902 10/15/2015

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

03/02/2020

STATE OR COUNTRY

UNITED STATES

ADDRESS

FOLEY & LARDNER LLP

3000 K STREET N.W.

SUITE 600

WASHINGTON, DC 20007-5109

UNITED STATES

FILING FEE RECEIVED

\$1,720

PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	3		

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			
	J1	17/487,698	09-28-2021	LUNDAHL ET AL.	
	J2	17/506,849	10-21-2021	BOYAJIAN 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 Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	J3	WO-96/06602-A1	03-07-1996	NOVEN PHARMA		

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 ⁶
	J4	Affidavit of Duncan Hall, August 10, 2021	
	J5	Agostinis et al. Photodynamic therapy of cancer: an update. CA: A Cancer Journal for Clinicians. 2011 May; 61(4):250-2	
	J6	Aktelite CL128 Operators Manual with Metvixia, Revised 2008	
	J7	Ameluz, Prescribing Information (2016)	
	J8	Berardesca E, Vignoli GP, Fideli D, Maibach H. Effect of occlusive dressings on the stratum corneum water holding capacity. The American Journal of the Medical Sciences. 1992 Jul;304(1):25-28	
	J9	Bissonnette R. Photodynamic therapy. In: Gold M.H., editor. Photodynamic Therapy in Dermatology. Springer Science and Business Media, LLC; New York, NY, USA: 2011. pp. 221-229	
	J10	Blu-U, Operating Manual (2006)	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	03/23/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
Sheet	2	of	3

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 ⁶
	J11	Calderhead RG. Light-emitting diode phototherapy in dermatological practice in lasers in dermatology and medicine. Lasers in Dermatology and Medicine. 2011 Aug;231-265	
	J12	CV of Dr. Howard Rogers MD, PHD	
	J13	Declaration of Dr. Howard Rogers MD, PHD, 10/19/2021	
	J14	DUSA Levulan Press Release, December 6, 1999	
	J15	European Medicines Agency CHMP Assessment Report (excerpts), October 20, 2011	
	J16	Fauteck Europe PMC Website Database Listing, 10/25/2007	
	J17	Fauteck JD, Ackermann G, Birkel M, Breuer M, Moor AC, Ebeling A, Ortlund C. Fluorescence characteristics and pharmacokinetic properties of a novel self-adhesive 5-ALA patch for photodynamic therapy of actinic keratoses, 2008.	
	J18	Harris DR. Percutaneous absorption and the surface area of occluded skin: a scanning electron microscopic study. British Journal of Dermatology. 1974; 91(27-32)	
	J19	Hongcharu W., Taylor C., Chang, Y., Aghasi, D., Suthamjariya, K., Anderson, R. Topical ALA-photodynamic therapy for the treatment of acne vulgaris. J Invest Dermatol. 2000 Aug;115(2):183-92	
	J20	International Patent Reviews, LLC review of U.S. Patent No. 10,357,567 dated July 26, 2021	
	J21	Jeffes E., McCullough J., Weinstein G., Fergin P., Nelson J., Shull T., Simpson K., Bukaty L., Hoffman W., Fong N. Photodynamic therapy of actinic keratosis with topical 5- aminolevulinic acid. A pilot dose-ranging study. Arch Dermatol. 1997	
	J22	Levulan, Label (2002)	
	J23	Levulan, Label (2009)	
	J24	MacCormack MA. Photodynamic therapy in dermatology: an update on applications and outcomes. Semin Cutan Med Surg. 2008 Mar;27(1):52-62	
	J25	McLaren G. Photodynamic therapy. In: Pfenninger and Fowler's procedures for primary care. Third Ed. Mosby Elsevier; Philadelphia, PA: 2011. pp 397-400	
	J26	News article entitled DUSA Pharmaceuticals To Pay U.S. \$20.75 Million To Settle False Claims Act Allegations Relating To Promotion Of Unsupported Drug Administration Process, August 24, 2020	
	J27	Ozog, D., Rkein, A., Fabi, S., Gold M., Goldman, M., Lowe, N., Martin, G., Munavalli, G. Photodynamic therapy: A clinical consensus guide. Dermatol Surg. 2016 Jul;42(7):804-27	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	03/23/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
Sheet	3	of	3

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 ⁶
	J28	Palm M., Goldman P.M. Aminolevulinic acid: actinic keratosis and photorejuvenation. In: Gold M.H., editor. Photodynamic Therapy in Dermatology. Springer Science and Business Media, LLC. 2011 Nov;5:30	
	J29	Petition for Inter Partes Review Under 35 U.S.C. 312, October 19, 2021	
	J30	Rick K, Sroka R, Stepp H, Kriegmair M, Huber RM, Jacob K, Baumgartner R. Pharmacokinetics of 5-aminolevulinic acid-induced protoporphyrin IX in skin and blood. J Photochem Photobiol B. 1997 Oct;40(3):313-9	
	J31	Sakamoto FH, Torezan L, Anderson RR. Photodynamic therapy for acne vulgaris: a critical review from basics to clinical practice: part II. Understanding parameters for acne treatment with photodynamic therapy. J Am Acad Dermatol. 2010 Aug;63(2):195-211	
	J32	Sotiriou E, Apalla Z, Maliamani F, Zapparas N, Panagiotidou D, Ioannides D. Intraindividual, right-left comparison of topical 5-aminolevulinic acid photodynamic therapy vs. 5% imiquimod cream for actinic keratoses on the upper extremities, 2009.	
	J33	Sotiriou Pubmed Website Database Listing, 09/23/2009	
	J34	Wachowska et al., Aminolevulinic acid (ALA) as a prodrug in photodynamic therapy of cancer. Molecules. 2011 May; 16(5): 4140-4164	
	J35	Wiley A, Anderson RR, Sakamoto FH. Temperature-modulated photodynamic therapy for the treatment of actinic keratosis on the extremities. Dermatologic Surgery. 2014 Oct;40(10):1094-1102	
	J36	Wiley Pubmed Website Database Listing, October 2014	
	J37	Wolf P., Rieger E. and Kerl H. Topical photodynamic therapy with endogenous porphyrins after application of 5-aminolevulinic acid: an alternative treatment modality for solar keratoses, superficial squamous cell carcinomas, and basal cell carcinomas?, January 1993	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	03/23/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: February 10, 2022 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			
	K1	2010/0174222-A1	07-08-2010	MCDANIEL, DAVID H.	
	K2	2015/0290470-A1	10-15-2015	TAPPER ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	K3	WO-2013/110021-A1	07-25-2013	HARVARD BIOSCIENCE INC , UNIV NEW YORK STATE RES FOUND		

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 ⁶
	K4	Japanese Office Action and English translation, Application No. 2019-555822, 1/11/2022, 13 pages	T
	K5	USPTO Office Action, 16/808,631 (067286-0409), 1/21/2022, 28 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	03/23/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: December 20, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			
	K1	11,135,293-B2	10-05-2021	LUNDAHL ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				

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 ⁶
	K2	Australian Examination Report, Application No. 2020267186, 11/19/2021, 6 pages	
	K3	USPTO Office Action, 17/487,698 (067286-0437), 12/17/2021, 21 pages	
	K4	Zhang et al., "Topical 5-Aminolevulinic Photodynamic Therapy with Red Light vs Intense Pulsed Light for the Treatment of Acne Vulgaris _ A Split Face, Randomized, Prospective Study," DERMATO-ENDOCRINOLOGY, 2018, VOL. 9, NO. 1, e1375634 (9 pages)	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	03/23/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: May 3, 2022 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

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)			
	M1	8,226,289-B2	07-24-2012	LINDEBERG	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	M2	Australian Examination Report, Application No. 2020267186, 2/3/2022, 4 pages	
	M3	Australian Examination Report, Application No. 2021107564, 4/4/2022, 4 pages	
	M4	Notice of Allowance, 17/487,698 (067286-0437), 04/29/2022, 11 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	05/06/2022
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PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	31	((("DUSA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2019/03/25 10:32 AM
L2	30	((("BOYAJIAN") near3 ("Thomas")) OR ((("CAROTA") near3 ("Mark")) OR ((("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 10:32 AM
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L72	1	("8021501").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/29 10:10 AM
L73	6919	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L74	11077	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L75	8626	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L76	2800	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L77	6742	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L78	578	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L79	1351	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L80	4117	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L81	1294	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L82	285	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM

L83	283	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L84	30469	L73 L74 L75 L76 L77 L78 L79 L80 L81 L82 L83	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L85	3612	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L86	31266	L84 L85	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L87	10	L86 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L88	618	L86 and ((sens\$6 determin\$6 detect\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:29 AM
L89	6941	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L90	11104	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L91	8674	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L92	2822	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L93	6752	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L94	581	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L95	1355	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L96	4132	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L97	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L98	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L99	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L100	30552	L89 L90 L91 L92 L93	(US-PGPUB; USPAT;	OR	ON	ON	2019/10/31

L101	3643	L94 L95 L96 L97 L98 L99 A61N2005/0662.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:34 PM 2019/10/31 01:34 PM
L102	31352	L100 L101	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L103	242	L102 and ((measur\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L104	6943	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L105	11105	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L106	8678	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L107	2825	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L108	6754	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L109	583	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L110	1356	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L111	4135	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L112	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L113	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L114	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L115	30563	L104 L105 L106 L107 L108 L109 L110 L111 L112 L113 L114	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L116	3643	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L117	31363	L115 L116	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2019/11/04 11:37 AM

L118	10	L117 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L124	1	("20120283328").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/01/31 08:26 AM
L125	22	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107- \$).did. or (US-9533170- \$).did. or (EP-2016977- \$ or WO-2018191356- \$).did. or (US- 20160175609-\$ or US- 20160175608-\$ or GB- 2501670-\$ or US- 20160175610-\$ or US- 20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/23 01:14 PM
L126	0	L125 and aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L127	0	L125 and ala	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L128	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L129	4618	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L130	2839	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L131	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L132	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L133	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L134	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM

L135	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L136	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L137	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L138	8097	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L139	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L140	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L141	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L142	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L143	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L144	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L145	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L146	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L147	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L148	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L149	36840	L138 L139 L140 L141 L142 L143 L144 L145 L146 L147 L148	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L150	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L151	37870	L149 L150	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L152	46164	L128 L129 L130 L131	(US-PGPUB; USPAT;	OR	ON	ON	2020/11/23

L153	845	L132 L133 L134 L135 L136 L137 L151 L152 and \$2aminolevulinic	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:05 PM 2020/11/23 03:07 PM
L154	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L155	4619	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L156	2842	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L157	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L158	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L159	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L160	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L161	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L162	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L163	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L164	8098	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L165	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L166	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L167	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L168	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L169	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2020/11/24 06:15 AM

L170	1645	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L171	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L172	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L173	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L174	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L175	36843	L164 L165 L166 L167 L168 L169 L170 L171 L172 L173 L174	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L176	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L177	37873	L175 L176	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L178	46171	L154 L155 L156 L157 L158 L159 L160 L161 L162 L163 L177	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L179	845	L178 and \$2aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L180	1	(10/466734).APP.	(USPAT; USOCR)	OR	ON	ON	2020/11/24 01:51 PM
L181	12	"19912039".FMID.	(US-PGPUB; USPAT; FPRS; JPO)	OR	ON	ON	2020/11/24 01:58 PM
L182	39	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/24 02:10 PM

L183	25	027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").P N. (US-20070283655-\$ or US-20130066405-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$).did. or (US-9227082-\$ or US-9017391-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/27 01:52 PM
L184	56	(US-0010591-\$ US-0031924-\$ US-0066405-\$ US-0067024-\$ US-0075703-\$ US-0088296-\$ US-0090877-\$ US-0106222-\$ US-0162109-\$ US-0162596-\$ US-0166846-\$ US-0174223-\$ US-0175609-\$ US-0175610-\$ US-0190845-\$ US-0238776-\$ US-0241726-\$ US-0253175-\$ US-0260365-\$ US-0283328-\$ US-0283655-\$ US-0287671-\$ US-0287696-\$ US-16787667-\$ US-20030088296-\$ US-20040162596-\$ US-20040260365-\$ US-	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:55 PM

		20050075703-\$ US- 20050090877-\$ US- 20060241726-\$ US- 20060253175-\$ US- 20060287696-\$ US- 20070283655-\$ US- 20080031924-\$ US- 20100010591-\$ US- 20100174223-\$ US- 20110106222-\$ US- 20120283328-\$ US- 20120287671-\$ US- 20130066405-\$ US- 20130190845-\$ US- 20140067024-\$ US- 20150162109-\$ US- 20150238776-\$ US- 20160166846-\$ US- 20160175609-\$ US- 20160175610-\$ US- 5814008-\$ US- 5849027-\$ US- 6223071-\$ US- 6709446-\$ US- 7190109-\$ US- 7723910-\$ US- 8030836-\$ US- 8216289-\$ US- 8758418-\$ US- 9533170-\$).DID.					
L185	6	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:59 PM
L186	1	("10357567").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/11/27 01:59 PM
L187	18	L183 not (L184 L185 L186)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/27 01:59 PM
L188	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L189	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L190	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L191	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L192	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L193	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/16

L194	5775	A61N2005/0651.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:49 PM 2021/03/16 12:49 PM
L195	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L196	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L197	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L198	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L199	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L200	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L201	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L202	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L203	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L204	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L205	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L206	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L207	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L208	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L209	38191	L198 L199 L200 L201 L202 L203 L204 L205 L206 L207 L208	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L210	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/16 12:49 PM

L211	39273	L209 L210	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L212	47948	L188 L189 L190 L191 L192 L193 L194 L195 L196 L197 L211	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L213	987	L212 and hinge	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L214	23	L212 and (((wide\$4 and narrow\$6) or (first and second)) adj width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:50 PM
L215	117	L212 and (((wide\$4 and narrow\$6) or (first and second)) near3 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:51 PM
L216	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L217	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L218	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L219	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L220	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L221	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L222	5775	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L223	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L224	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L225	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L226	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L227	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM

L228	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L229	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L230	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L231	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L232	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L233	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L234	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L235	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L236	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L237	38191	L226 L227 L228 L229 L230 L231 L232 L233 L234 L235 L236	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L238	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L239	39273	L237 L238	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L240	47948	L216 L217 L218 L219 L220 L221 L222 L223 L224 L225 L239	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L241	199	L240 and (((wide\$4 and narrow\$6) or (first and second)) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L242	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L243	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L244	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L245	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/18

L246	757	A61N2005/0633.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	09:35 AM 2021/03/18 09:35 AM
L247	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L248	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L249	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L250	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L251	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L252	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L253	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L254	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L255	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L256	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L257	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L258	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L259	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L260	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L261	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L262	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/18 09:35 AM

L263	38197	L252 L253 L254 L255 L256 L257 L258 L259 L260 L261 L262	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L264	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L265	39279	L263 L264	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L266	47959	L242 L243 L244 L245 L246 L247 L248 L249 L250 L251 L265	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L267	199	L266 and (((wide\$4 and narrow\$6) or (first and second))) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L268	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L269	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L270	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L271	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L272	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L273	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L274	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L275	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L276	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L277	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L278	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L279	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM

L280	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L281	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L282	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L283	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L284	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L285	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L286	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L287	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L288	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L289	38197	L278 L279 L280 L281 L282 L283 L284 L285 L286 L287 L288	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L290	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L291	39279	L289 L290	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L292	47959	L268 L269 L270 L271 L272 L273 L274 L275 L276 L277 L291	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L293	0	2007/112427	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:22 PM
L294	582470	(stephen tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L295	242	(stephen and tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L296	10	("0000001" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM

L297	2	("5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L298	3	("0000002" "D000001").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L299	10	("5032400" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:14 PM
L300	1	("20110224598").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2021/07/07 03:15 PM
L301	3	("0000001" "7033381" "7730893").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:16 PM
L302	14	L299 L300 L301	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:16 PM
L303	9	L302 and (wid\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:18 PM
L304	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L305	4963	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L306	3093	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L307	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L308	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L309	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L310	5920	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L311	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L312	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L313	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM

L314	8498	A61N5/06.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L315	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L316	11425	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L317	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L318	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L319	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L320	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L321	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L322	1468	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L323	399	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L324	469	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L325	38854	L314 L315 L316 L317 L318 L319 L320 L321 L322 L323 L324	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L326	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L327	39953	L325 L326	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L328	48853	L304 L305 L306 L307 L308 L309 L310 L311 L312 L313 L327	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L329	217	L328 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:21 PM
L331	3	("0000001" "0000002" "	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26

L332	2	20200100997").PN. (("20160346392") or ("20200100997")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	12:36 PM
L333	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:37 PM
L334	5141	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L335	3204	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L336	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L337	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L338	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L339	6128	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L340	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L341	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L342	6224	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L343	8694	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L344	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L345	11742	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L346	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L347	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L348	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L349	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/08/26

L350	6224	A61N2005/0663.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:42 PM 2021/08/26 12:42 PM
L351	1481	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L352	408	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L353	492	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L354	39744	L343 L344 L345 L346 L347 L348 L349 L350 L351 L352 L353	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L355	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L356	40873	L354 L355	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L357	50063	L333 L334 L335 L336 L337 L338 L339 L340 L341 L342 L356	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L358	222	L357 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L360	37	((("DUSA") near3 ("PHARMACEUTICALS ") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2021/10/18 03:52 PM
L361	38	((("BOYAJIAN") near3 ("Thomas")) OR (("CAROTA") near3 ("Mark")) OR (("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:52 PM
L362	64	("0000002" "0000011" "20200100997" "0000001" "20190290763" "20200269063" "20200398071" "7730893" "20090247932" "20110224598" "20130274834" "20130289089" "20150290028" "20160008623" "20200261580" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20	(US-PGPUB; USPAT)	OR	ON	ON	2021/10/18 03:52 PM

		160045757" "5601838" "5686065" "6897238" "0 017109" "20010021812 " "D000001" "20040010 299" "20090324727" "2 0110053965" "2014001 0761" "20030088296" " 20040162596" "200402 60365" "20050075703" " "20050090877" "20060 241726" "20060253175 " "20060287696" "2007 0283655" "2008003192 4" "20100010591" "201 00174223" "201101062 22" "20120283328" "20 120287671" "20130066 405" "20130190845" "2 0140067024" "2015016 2109" "20150238776" " 20160166846" "201601 75609" "5849027" "622 3071" "6709446" "7156 865" "7190109" "77239 10" "8030836" "821628 9" "8758418" "9108045" "9533170").PN.					
L363	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L364	5189	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L365	3246	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L366	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L367	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L368	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L369	6171	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L370	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L371	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L372	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18

L373	8738	A61N5/06.cpc.	USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:53 PM
L374	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L375	11844	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L376	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L377	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L378	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L379	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L380	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L381	1484	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L382	413	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L383	498	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L384	39984	L373 L374 L375 L376 L377 L378 L379 L380 L381 L382 L383	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L385	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L386	41124	L384 L385	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L387	50408	L363 L364 L365 L366 L367 L368 L369 L370 L371 L372 L386	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L388	3097	L387 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L389	29	(US-20070283655-\$ or US-20130066405-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM

		US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.					
L390	10	L389 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM
L391	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L392	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L393	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L394	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L395	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L396	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L397	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L398	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L399	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM

L400	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L401	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L402	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L403	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L404	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L405	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L406	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L407	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L408	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L409	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L410	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L411	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L412	40271	L401 L402 L403 L404 L405 L406 L407 L408 L409 L410 L411	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L413	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L414	41417	L412 L413	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L415	50819	L391 L392 L393 L394 L395 L396 L397 L398 L399 L400 L414	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L416	15	L415 and (nest\$6 near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L417	7	L415 and (recess\$6	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/19

		near3 hing\$9)	USOCR; FPRS; EPO; JPO; DERWENT)				10:30 AM
L418	0	L415 and (hidden near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:30 AM
L419	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L420	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L421	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L422	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L423	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L424	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L425	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L426	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L427	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L428	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L429	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L430	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L431	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L432	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L433	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L434	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM

L435	1805	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L436	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L437	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L438	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L439	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L440	40271	L429 L430 L431 L432 L433 L434 L435 L436 L437 L438 L439	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L441	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L442	41417	L440 L441	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L443	50819	L419 L420 L421 L422 L423 L424 L425 L426 L427 L428 L442	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L444	59	L443 and (dead near3 space)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L445	61	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:51 PM
L446	66	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9 decreas\$6))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L447	112	L444 L445 L446	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L448	30	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM

		US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L449	17	L448 and output	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM
L450	19	L448 and (shape size measur\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:45 PM
L451	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L452	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L453	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L454	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L455	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L456	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L457	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L458	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L459	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L460	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L461	8783	A61N5/06.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/20

L462	14390	A61N5/062.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:49 PM 2021/10/20 01:49 PM
L463	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L464	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L465	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L466	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L467	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L468	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L469	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L470	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L471	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L472	40271	L461 L462 L463 L464 L465 L466 L467 L468 L469 L470 L471	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L473	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L474	41417	L472 L473	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L475	50819	L451 L452 L453 L454 L455 L456 L457 L458 L459 L460 L474	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L476	1292	L475 and ((sens\$6 detect\$6) near5 (shape size))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L477	45	L475 and ((sens\$6 detect\$6) with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:51 PM
L478	54	L475 and ((sens\$6	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/20

		detect\$6 measur\$6) with (shape size) with (treatment adj (surface area)))	USOCR; FPRS; EPO; JPO; DERWENT)				01:54 PM
L479	162	L475 and ((sens\$6 detect\$6 measur\$6 adjust adjusting adjusted adjustable "based on") with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:58 PM
L480	88	L479 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:59 PM
L481	17	L448 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L482	0	L448 and ("j/cm" "mw/cm")	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L483	7	L475 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:47 PM
L484	46	L475 and ("j/cm" "mw/cm" (nm or nanometer))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:48 PM
L485	34	L484 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:48 PM
L486	629	L475 and (intensity with red) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L487	442	L475 and (intensity with red with light) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L488	0	L475 and (intensity with red with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L489	7	L475 and (intensity with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L490	32	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM

		US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$ or US-20130066404-\$ or US-20030216795-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L491	20	L490 and intensity	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM
L492	3	("0000002" OR "0017487" OR "0017506").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L493	2	("0000001" OR "0000002").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L494	3	("0000001" OR "0000002" OR "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L495	3	("11135293" "20100174222" "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:17 AM
L496	53969	A61N5/062,06,0616.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:37 PM
L497	40946	A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL,	OR	ON	ON	2022/03/23 03:38 PM

L498	13206	A61B5/0064,0082.cpc.	NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L499	85960	496 497 498	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L500	20151	499 AND (intensity WITH light)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:39 PM
L501	7575	499 AND (intensity WITH light WITH (more	(US-PGPUB; USPAT; USOCR; FIT (AP, AT,	OR	ON	ON	2022/03/23 03:40 PM

		less higher lower highest lowest greater))	AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L502	2876	499 AND (intensity WITH light WITH (more less higher lower highest lowest greater))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:47 PM
L503	4680	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L504	1777	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L505	4689	501 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:25 PM
L508	408	L505 AND hing\$6	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY,	OR	ON	ON	2022/05/06 02:47 PM

L509	116	((US-20130190845-A1 OR US-20120148975-A1 OR US-20130196284-A1 OR US-20120148976-A1 OR US-20100179622-A1 OR US-20130280671-A1 OR US-20140072932-A1 OR US-20050004632-A1 OR US-20070248930-A1 OR US-20150140502-A1 OR US-20110176326-A1 OR US-20070129776-A1 OR US-20020035386-A1 OR US-20020120312-A1 OR US-20070283655-A1 OR US-20120150265-A1 OR US-20160129279-A1 OR US-20140277291-A1 OR US-20130303972-A1 OR US-20020029071-A1 OR US-20070150031-A1 OR US-20130079759-A1 OR US-20130178919-A1 OR US-20160158485-A1 OR US-20160175609-A1 OR US-20100030013-A1 OR US-20090054953-A1 OR US-20040249423-A1 OR US-20160101295-A1 OR US-20030004499-A1 OR US-20120330386-A1 OR US-20090005839-A1 OR US-20140187998-A1 OR US-20160325109-A1	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); USPAT; DERWENT)	OR	ON	ON	2022/05/06 02:53 PM
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L511	408	<p>9013701-B2 OR US-9175945-B2 OR US-9448061-B2 OR US-7544204-B2 OR US-10238294-B2 OR US-9907688-B2 OR US-8380291-B2 OR US-8391960-B2 OR US-8706200-B2 OR US-8838210-B2 OR US-9186063-B2 OR US-9226664-B2 OR US-10052393-B2 OR US-10357662-B2 OR US-10194808-B1 OR US-8528563-B2 OR US-9301770-B2 OR US-10165976-B2 OR US-9700342-B2).did. AND USPT.dbnm.) OR ((WO-2012075584-A1).did. AND DWPI.dbnm.)</p> <p>L510 AND (intensity WITH light WITH (more less higher lower highest lowest greater))</p>	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:55 PM
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PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N119	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:19 AM
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N121	189	(panel AND width AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N122	213	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N123	3	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:38 AM
N330	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 07:14 PM
N359	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26 12:42 PM
N361	3	(panel AND (width wide wider longer long short shorter bigger) AND ((light illuminat\$6 led) WITH intens\$6) AND (nest\$6 WITH hing\$6)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/05/06 02:49 PM

PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: April 4, 2022 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
Sheet	1	of	1

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ - Kind Code ⁵ (if known)				

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 ⁶
	L1	MAISCH ET AL., Fluorescence Induction of Protoporphyrin IX by a New 5-Aminolevulinic Acid Nanoemulsion Used for Photodynamic Therapy in a Full-Thickness ex vivo Skin Model, Experimental Dermatology, 19, 2009, pp. e302-e305	
	L2	NUCCI ET AL., Treatment of Anogenital Condylomata Acuminata with Topical Photodynamic Therapy: Report of 14 Cases and Review, International Journal of Infectious Diseases, 14S, 2010, pp. e280-e282	
	L3	USPTO Non-Final Office Action, 16/631,205 (067286-0423), 03/03/2022, 31 pages	
	L4	WILLEY ET AL., American Society for Laser Medicine and Surgery Abstracts, #147, Ultra Fast Thermal PDT for Facial AKs: Proof of Concept Study, March 2017, 2 pages	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	05/06/2022
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	05/20/2022		
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			05/20/2022	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):

ipdocketing@foley.com

Corrected Notice of Allowability	Application No. 16/791,004	Applicant(s) Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the interview conducted on 5/17/2022.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2. ☐ 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.

3. ☒ The allowed claim(s) is/are 1-6 and 11-24. As a result of the allowed claim(s), 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.

4. ☐ 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)).

* Certified copies not received: ____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date ____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date ____. 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material ____. 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date. <u>20220517</u> .	5. ☐ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/TAMMIE K MARLEN/
 Primary Examiner, Art Unit 3792

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.

Information Disclosure Statement

2. The information disclosure statement(s) (IDS) submitted on November 18, 2021 has/have been acknowledged and is/are being considered by the Examiner.

Allowable Subject Matter

3. Claims 1-6 and 11-24 are allowed.

4. The following is an examiner's statement of reasons for allowance: It is in the opinion of the examiner that the art of record neither anticipates nor renders obvious "nested hinges on inner side surfaces of adjacent panels" and "wherein each of the at least five panels has two first edges and two second edges shorter than the two first edges, and the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges" in combination with the rest of the claimed limitations set forth in the independent claim.

Searching by the Examiner yielded prior art as cited in the previous Office Actions. Based on Applicant's arguments and the Examiner's review of the Office Action mailed on October 25, 2021, the subject matter is deemed to be allowable. Further explanation can be reviewed in the Applicant's arguments filed on February 25, 2022. Therefore, it is concluded by the examiner that claims 1-6 and 11-24 of the present invention are allowable..

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAMMIE K MARLEN whose telephone number is (571)272-1986. The examiner can normally be reached Monday through Friday from 8 am until 4 pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on 571-272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TAMMIE K MARLEN/
Primary Examiner, Art Unit 3792

<i>Applicant-Initiated Interview Summary</i>	Application No. 16/791,004	Applicant(s) Boyajian et al.		
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
TAMMIE K MARLEN	Primary Examiner	Telephonic
Kiri Lee Sharon	Attorney of Record	

Date of Interview: 17 May 2022

Issues Discussed:

Other

Applicant's representative contacted the Examiner regarding the references lined through on the IDS of 11/18/2021. Applicant's representative indicated that copies of the lined-through unpublished applications are not required to be provided because the unpublished applications are available in IFW. (see MPEP 609.04(a)(II)(C)) The Examiner agreed and indicated that a Corrected Notice of Allowability will be issued.

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
<p>Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04</p> <p>Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing</p>	

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.

Search Notes 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

CPC - Searched*		
Symbol	Date	Examiner
A61N 5/06,062,0616	10/20/2021	TKM
A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662	10/20/2021	TKM
A61B5/0064,0082	10/20/2021	TKM
Updated above	05/06/2022	TKM

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name and assignee search	10/20/2021	TKM
Text-limited and related application search – see search history printout	10/20/2021	TKM
Consulted Alyssa Alter	10/20/2021	TKM
Updated above	05/06/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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<i>Search Notes</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	PGPUB text search -- see interference search printout	05/06/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	

CPC						
Symbol					Type	Version
A61N	/	5	/	062	F	2013-01-01
A61B	/	5	/	0064	I	2013-01-01
A61B	/	5	/	0082	I	2013-01-01
A61N	/	2005	/	0633	A	2013-01-01
A61N	/	2005	/	0626	A	2013-01-01
A61N	/	2005	/	0642	A	2013-01-01
A61N	/	2005	/	0652	A	2013-01-01
A61N	/	2005	/	0663	A	2013-01-01
A61N	/	2005	/	0662	A	2013-01-01
A61N	/	2005	/	0651	A	2013-01-01

CPC Combination Sets					
Symbol				Type	Set
	/		/		

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) _____		17 May 2022 (Date)	O.G. Print Claim(s) 1 O.G. Print Figure 2A

<i>Issue Classification</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61N5/06	/	5	/ 06
NON-CLAIMED			
/	/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	17 May 2022	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	2A

Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1		10	17	19										
2	2	9	11	19	20										
3	3	12	12	6	21										
4	4	15	13	18	22										
5	5	10	14	7	23										
8	6	13	15	20	24										
	7	11	16												
	8	14	17												
	9	16	18												

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) 17 May 2022		O.G. Print Claim(s) 1	O.G. Print Figure 2A

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	31	((("DUSA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2019/03/25 10:32 AM
L2	30	((("BOYAJIAN") near3 ("Thomas")) OR ((("CAROTA") near3 ("Mark")) OR ((("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 10:32 AM
L3	6	("0000002" "0000003" "0000004" "0000005" "0000006" "0000007").PN	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L6	4	("0000001" "0000002" "0000003" "0000004").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L7	14	("0000001" "0000002" "0000003" "0000004" "20040162596" "20040260365" "5814008" "5849027" "9108045" "20050075703" "20060241726" "0000005" "0000006" "0000007").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L8	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 10:37 AM
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L10	9	((("20030088296") or ("20050090877") or ("20060253175") or ("20070283655") or ("20100010591") or ("20110106222") or ("20140067024") or ("9533170")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 01:12 PM
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L12	14	(US-0162109-\$ US-0287671-\$ US-0287696-\$ US-	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 01:16 PM

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L20	4	("0000001" "0000002" "0000003" "0000004").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM
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L22	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:01 PM
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L32	5	L16	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L33	11523	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L34	8633	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L35	2743	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L36	6725	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L37	572	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L38	1341	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L39	4107	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L40	1289	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L41	285	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM

L42	282	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM
L43	30801	L31 L33 L34 L35 L36 L37 L38 L39 L40 L41 L42	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM
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L45	31604	L43 L44	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:10 PM
L46	8642	L45 and (diode led)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:10 PM
L47	280	(L41 L37) and (L36 L39 L44 (diode led))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:18 PM
L48	280	(L41 L37) and (L36 L39 L44 (diode led))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:18 PM
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L62	1341	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
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L65	285	A61N2005/064.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2019/03/29

L66	282	A61N2005/0658.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	08:56 AM 2019/03/29 08:56 AM
L67	30814	L56 L57 L58 L59 L60 L61 L62 L63 L64 L65 L66	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L68	3653	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L69	31617	L67 L68	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L70	2785	L69 and (panel\$4 hing\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L71	45	L69 and ((five fifth) with (panel\$4 hing\$6))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:58 AM
L72	1	("8021501").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/29 10:10 AM
L73	6919	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L74	11077	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L75	8626	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L76	2800	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L77	6742	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L78	578	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L79	1351	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L80	4117	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L81	1294	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L82	285	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM

L83	283	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L84	30469	L73 L74 L75 L76 L77 L78 L79 L80 L81 L82 L83	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L85	3612	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L86	31266	L84 L85	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L87	10	L86 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L88	618	L86 and ((sens\$6 determin\$6 detect\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:29 AM
L89	6941	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L90	11104	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L91	8674	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L92	2822	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L93	6752	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L94	581	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L95	1355	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L96	4132	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L97	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L98	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L99	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L100	30552	L89 L90 L91 L92 L93	(US-PGPUB; USPAT;	OR	ON	ON	2019/10/31

L101	3643	L94 L95 L96 L97 L98 L99 A61N2005/0662.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:34 PM 2019/10/31 01:34 PM
L102	31352	L100 L101	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L103	242	L102 and ((measur\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L104	6943	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L105	11105	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L106	8678	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L107	2825	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L108	6754	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L109	583	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L110	1356	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L111	4135	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L112	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L113	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L114	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L115	30563	L104 L105 L106 L107 L108 L109 L110 L111 L112 L113 L114	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L116	3643	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L117	31363	L115 L116	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2019/11/04 11:37 AM

L118	10	L117 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L124	1	("20120283328").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/01/31 08:26 AM
L125	22	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107- \$).did. or (US-9533170- \$).did. or (EP-2016977- \$ or WO-2018191356- \$).did. or (US- 20160175609-\$ or US- 20160175608-\$ or GB- 2501670-\$ or US- 20160175610-\$ or US- 20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/23 01:14 PM
L126	0	L125 and aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L127	0	L125 and ala	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L128	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L129	4618	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L130	2839	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L131	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L132	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L133	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L134	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM

L135	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L136	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L137	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L138	8097	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L139	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L140	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L141	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L142	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L143	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L144	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L145	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L146	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L147	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L148	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L149	36840	L138 L139 L140 L141 L142 L143 L144 L145 L146 L147 L148	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L150	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L151	37870	L149 L150	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L152	46164	L128 L129 L130 L131	(US-PGPUB; USPAT;	OR	ON	ON	2020/11/23

L153	845	L132 L133 L134 L135 L136 L137 L151 L152 and \$2aminolevulinic	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:05 PM 2020/11/23 03:07 PM
L154	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L155	4619	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L156	2842	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L157	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L158	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L159	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L160	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L161	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L162	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L163	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L164	8098	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L165	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L166	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L167	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L168	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L169	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2020/11/24 06:15 AM

L170	1645	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L171	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L172	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L173	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L174	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L175	36843	L164 L165 L166 L167 L168 L169 L170 L171 L172 L173 L174	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L176	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L177	37873	L175 L176	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L178	46171	L154 L155 L156 L157 L158 L159 L160 L161 L162 L163 L177	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L179	845	L178 and \$2aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L180	1	(10/466734).APP.	(USPAT; USOCR)	OR	ON	ON	2020/11/24 01:51 PM
L181	12	"19912039".FMID.	(US-PGPUB; USPAT; FPRS; JPO)	OR	ON	ON	2020/11/24 01:58 PM
L182	39	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/24 02:10 PM

L183	25	027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").P N. (US-20070283655-\$ or US-20130066405-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$).did. or (US-9227082-\$ or US-9017391-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/27 01:52 PM
L184	56	(US-0010591-\$ US-0031924-\$ US-0066405-\$ US-0067024-\$ US-0075703-\$ US-0088296-\$ US-0090877-\$ US-0106222-\$ US-0162109-\$ US-0162596-\$ US-0166846-\$ US-0174223-\$ US-0175609-\$ US-0175610-\$ US-0190845-\$ US-0238776-\$ US-0241726-\$ US-0253175-\$ US-0260365-\$ US-0283328-\$ US-0283655-\$ US-0287671-\$ US-0287696-\$ US-16787667-\$ US-20030088296-\$ US-20040162596-\$ US-20040260365-\$ US-	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:55 PM

		20050075703-\$ US- 20050090877-\$ US- 20060241726-\$ US- 20060253175-\$ US- 20060287696-\$ US- 20070283655-\$ US- 20080031924-\$ US- 20100010591-\$ US- 20100174223-\$ US- 20110106222-\$ US- 20120283328-\$ US- 20120287671-\$ US- 20130066405-\$ US- 20130190845-\$ US- 20140067024-\$ US- 20150162109-\$ US- 20150238776-\$ US- 20160166846-\$ US- 20160175609-\$ US- 20160175610-\$ US- 5814008-\$ US- 5849027-\$ US- 6223071-\$ US- 6709446-\$ US- 7190109-\$ US- 7723910-\$ US- 8030836-\$ US- 8216289-\$ US- 8758418-\$ US- 9533170-\$).DID.					
L185	6	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:59 PM
L186	1	("10357567").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/11/27 01:59 PM
L187	18	L183 not (L184 L185 L186)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/27 01:59 PM
L188	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L189	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L190	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L191	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L192	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L193	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/16

L194	5775	A61N2005/0651.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:49 PM 2021/03/16 12:49 PM
L195	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L196	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L197	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L198	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L199	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L200	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L201	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L202	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L203	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L204	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L205	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L206	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L207	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L208	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L209	38191	L198 L199 L200 L201 L202 L203 L204 L205 L206 L207 L208	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L210	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/16 12:49 PM

L211	39273	L209 L210	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L212	47948	L188 L189 L190 L191 L192 L193 L194 L195 L196 L197 L211	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L213	987	L212 and hinge	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L214	23	L212 and (((wide\$4 and narrow\$6) or (first and second)) adj width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:50 PM
L215	117	L212 and (((wide\$4 and narrow\$6) or (first and second)) near3 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:51 PM
L216	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L217	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L218	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L219	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L220	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L221	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L222	5775	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L223	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L224	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L225	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L226	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L227	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM

L228	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L229	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L230	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L231	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L232	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L233	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L234	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L235	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L236	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L237	38191	L226 L227 L228 L229 L230 L231 L232 L233 L234 L235 L236	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L238	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L239	39273	L237 L238	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L240	47948	L216 L217 L218 L219 L220 L221 L222 L223 L224 L225 L239	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L241	199	L240 and (((wide\$4 and narrow\$6) or (first and second)) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L242	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L243	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L244	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L245	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/18

L246	757	A61N2005/0633.cpc.	USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	09:35 AM
L247	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L248	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L249	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L250	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L251	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L252	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L253	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L254	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L255	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L256	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L257	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L258	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L259	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L260	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L261	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L262	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/18 09:35 AM

L263	38197	L252 L253 L254 L255 L256 L257 L258 L259 L260 L261 L262	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L264	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L265	39279	L263 L264	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L266	47959	L242 L243 L244 L245 L246 L247 L248 L249 L250 L251 L265	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L267	199	L266 and (((wide\$4 and narrow\$6) or (first and second))) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L268	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L269	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L270	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L271	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L272	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L273	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L274	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L275	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L276	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L277	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L278	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L279	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM

L280	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L281	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L282	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L283	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L284	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L285	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L286	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L287	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L288	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L289	38197	L278 L279 L280 L281 L282 L283 L284 L285 L286 L287 L288	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L290	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L291	39279	L289 L290	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L292	47959	L268 L269 L270 L271 L272 L273 L274 L275 L276 L277 L291	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L293	0	2007/112427	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:22 PM
L294	582470	(stephen tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L295	242	(stephen and tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L296	10	("0000001" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM

L297	2	("5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L298	3	("0000002" "D000001").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L299	10	("5032400" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:14 PM
L300	1	("20110224598").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2021/07/07 03:15 PM
L301	3	("0000001" "7033381" "7730893").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:16 PM
L302	14	L299 L300 L301	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:16 PM
L303	9	L302 and (wid\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:18 PM
L304	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L305	4963	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L306	3093	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L307	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L308	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L309	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L310	5920	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L311	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L312	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L313	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM

L314	8498	A61N5/06.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L315	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L316	11425	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L317	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L318	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L319	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L320	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L321	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L322	1468	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L323	399	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L324	469	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L325	38854	L314 L315 L316 L317 L318 L319 L320 L321 L322 L323 L324	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L326	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L327	39953	L325 L326	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L328	48853	L304 L305 L306 L307 L308 L309 L310 L311 L312 L313 L327	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L329	217	L328 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:21 PM
L331	3	("0000001" "0000002" "	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26

L332	2	20200100997").PN. (("20160346392") or ("20200100997")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	12:36 PM
L333	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:37 PM
L334	5141	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L335	3204	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L336	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L337	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L338	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L339	6128	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L340	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L341	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L342	6224	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L343	8694	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L344	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L345	11742	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L346	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L347	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L348	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L349	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/08/26

L350	6224	A61N2005/0663.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:42 PM 2021/08/26 12:42 PM
L351	1481	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L352	408	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L353	492	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L354	39744	L343 L344 L345 L346 L347 L348 L349 L350 L351 L352 L353	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L355	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L356	40873	L354 L355	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L357	50063	L333 L334 L335 L336 L337 L338 L339 L340 L341 L342 L356	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L358	222	L357 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L360	37	((("DUSA") near3 ("PHARMACEUTICALS ") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2021/10/18 03:52 PM
L361	38	((("BOYAJIAN") near3 ("Thomas")) OR (("CAROTA") near3 ("Mark")) OR (("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:52 PM
L362	64	("0000002" "0000011" "20200100997" "0000001" "20190290763" "20200269063" "20200398071" "7730893" "20090247932" "20110224598" "20130274834" "20130289089" "20150290028" "20160008623" "20200261580" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20	(US-PGPUB; USPAT)	OR	ON	ON	2021/10/18 03:52 PM

		160045757" "5601838" "5686065" "6897238" "0017109" "20010021812" "D000001" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").PN.					
L363	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L364	5189	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L365	3246	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L366	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L367	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L368	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L369	6171	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L370	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L371	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L372	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/18

L373	8738	A61N5/06.cpc.	USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:53 PM
L374	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L375	11844	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L376	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L377	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L378	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L379	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L380	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L381	1484	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L382	413	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L383	498	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L384	39984	L373 L374 L375 L376 L377 L378 L379 L380 L381 L382 L383	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L385	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L386	41124	L384 L385	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L387	50408	L363 L364 L365 L366 L367 L368 L369 L370 L371 L372 L386	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L388	3097	L387 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L389	29	(US-20070283655-\$ or US-20130066405-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM

		US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.					
L390	10	L389 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM
L391	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L392	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L393	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L394	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L395	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L396	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L397	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L398	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L399	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM

L400	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L401	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L402	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L403	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L404	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L405	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L406	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L407	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L408	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L409	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L410	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L411	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L412	40271	L401 L402 L403 L404 L405 L406 L407 L408 L409 L410 L411	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L413	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L414	41417	L412 L413	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L415	50819	L391 L392 L393 L394 L395 L396 L397 L398 L399 L400 L414	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L416	15	L415 and (nest\$6 near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L417	7	L415 and (recess\$6	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM

		near3 hing\$9)	USOCR; FPRS; EPO; JPO; DERWENT)				10:30 AM
L418	0	L415 and (hidden near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:30 AM
L419	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L420	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L421	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L422	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L423	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L424	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L425	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L426	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L427	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L428	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L429	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L430	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L431	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L432	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L433	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L434	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM

L435	1805	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L436	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L437	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L438	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L439	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L440	40271	L429 L430 L431 L432 L433 L434 L435 L436 L437 L438 L439	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L441	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L442	41417	L440 L441	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L443	50819	L419 L420 L421 L422 L423 L424 L425 L426 L427 L428 L442	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L444	59	L443 and (dead near3 space)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L445	61	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:51 PM
L446	66	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9 decreas\$6))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L447	112	L444 L445 L446	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L448	30	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM

		US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L449	17	L448 and output	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM
L450	19	L448 and (shape size measur\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:45 PM
L451	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L452	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L453	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L454	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L455	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L456	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L457	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L458	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L459	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L460	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L461	8783	A61N5/06.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/20

L462	14390	A61N5/062.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:49 PM 2021/10/20 01:49 PM
L463	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L464	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L465	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L466	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L467	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L468	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L469	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L470	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L471	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L472	40271	L461 L462 L463 L464 L465 L466 L467 L468 L469 L470 L471	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L473	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L474	41417	L472 L473	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L475	50819	L451 L452 L453 L454 L455 L456 L457 L458 L459 L460 L474	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L476	1292	L475 and ((sens\$6 detect\$6) near5 (shape size))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L477	45	L475 and ((sens\$6 detect\$6) with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:51 PM
L478	54	L475 and ((sens\$6	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/20

		detect\$6 measur\$6) with (shape size) with (treatment adj (surface area)))	USOCR; FPRS; EPO; JPO; DERWENT)				01:54 PM
L479	162	L475 and ((sens\$6 detect\$6 measur\$6 adjust adjusting adjusted adjustable "based on") with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:58 PM
L480	88	L479 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:59 PM
L481	17	L448 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L482	0	L448 and ("j/cm" "mw/cm")	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L483	7	L475 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:47 PM
L484	46	L475 and ("j/cm" "mw/cm" (nm or nanometer))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:48 PM
L485	34	L484 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:48 PM
L486	629	L475 and (intensity with red) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L487	442	L475 and (intensity with red with light) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L488	0	L475 and (intensity with red with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L489	7	L475 and (intensity with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L490	32	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM

		US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$ or US-20130066404-\$ or US-20030216795-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L491	20	L490 and intensity	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM
L492	3	("0000002" OR "0017487" OR "0017506").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L493	2	("0000001" OR "0000002").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L494	3	("0000001" OR "0000002" OR "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L495	3	("11135293" "20100174222" "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:17 AM
L496	53969	A61N5/062,06,0616.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:37 PM
L497	40946	A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL,	OR	ON	ON	2022/03/23 03:38 PM

L498	13206	A61B5/0064,0082.cpc.	NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L499	85960	496 497 498	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L500	20151	499 AND (intensity WITH light)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:39 PM
L501	7575	499 AND (intensity WITH light WITH (more	(US-PGPUB; USPAT; USOCR; FIT (AP, AT,	OR	ON	ON	2022/03/23 03:40 PM

		less higher lower highest lowest greater))	AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L502	2876	499 AND (intensity WITH light WITH (more less higher lower highest lowest greater))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:47 PM
L503	4680	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L504	1777	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L505	4689	501 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:25 PM
L508	408	L505 AND hing\$6	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY,	OR	ON	ON	2022/05/06 02:47 PM

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L511	408	<p>9013701-B2 OR US-9175945-B2 OR US-9448061-B2 OR US-7544204-B2 OR US-10238294-B2 OR US-9907688-B2 OR US-8380291-B2 OR US-8391960-B2 OR US-8706200-B2 OR US-8838210-B2 OR US-9186063-B2 OR US-9226664-B2 OR US-10052393-B2 OR US-10357662-B2 OR US-10194808-B1 OR US-8528563-B2 OR US-9301770-B2 OR US-10165976-B2 OR US-9700342-B2).did. AND USPT.dbnm.) OR ((WO-2012075584-A1).did. AND DWPI.dbnm.)</p> <p>L510 AND (intensity WITH light WITH (more less higher lower highest lowest greater))</p>	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:55 PM
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PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N119	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:19 AM
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N121	189	(panel AND width AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N122	213	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N123	3	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:38 AM
N330	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 07:14 PM
N359	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26 12:42 PM
N361	3	(panel AND (width wide wider longer long short shorter bigger) AND ((light illuminat\$6 led) WITH intens\$6) AND (nest\$6 WITH hing\$6)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2022/05/06 02:49 PM

PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	MARLEN, TAMMIE K				
Attorney Docket Number	067286-0410				
Sheet	1	of	3		

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)			

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Serial Number-Kind Code ² (if known)			
	J1	17/487,698	09-28-2021	LUNDAHL ET AL.	
	J2	17/506,849	10-21-2021	BOYAJIAN 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 Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	J3	WO-96/06602-A1	03-07-1996	NOVEN PHARMA		

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 ⁶
	J4	Affidavit of Duncan Hall, August 10, 2021	
	J5	Agostinis et al. Photodynamic therapy of cancer: an update. CA: A Cancer Journal for Clinicians. 2011 May; 61(4):250-2	
	J6	Aktelite CL128 Operators Manual with Metvixia, Revised 2008	
	J7	Ameluz, Prescribing Information (2016)	
	J8	Berardesca E, Vignoli GP, Fideli D, Maibach H. Effect of occlusive dressings on the stratum corneum water holding capacity. The American Journal of the Medical Sciences. 1992 Jul;304(1):25-28	
	J9	Bissonnette R. Photodynamic therapy. In: Gold M.H., editor. Photodynamic Therapy in Dermatology. Springer Science and Business Media, LLC; New York, NY, USA: 2011. pp. 221-229	
	J10	Blu-U, Operating Manual (2006)	

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	05/17/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
Sheet	2	of	3

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 ⁶
	J11	Calderhead RG. Light-emitting diode phototherapy in dermatological practice in lasers in dermatology and medicine. Lasers in Dermatology and Medicine. 2011 Aug;231-265	
	J12	CV of Dr. Howard Rogers MD, PHD	
	J13	Declaration of Dr. Howard Rogers MD, PHD, 10/19/2021	
	J14	DUSA Levulan Press Release, December 6, 1999	
	J15	European Medicines Agency CHMP Assessment Report (excerpts), October 20, 2011	
	J16	Fauteck Europe PMC Website Database Listing, 10/25/2007	
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Examiner Signature	/TAMMIE K MARLEN/	Date Considered	05/17/2022
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: November 18, 2021 <i>(use as many sheets as necessary)</i>		Complete if Known	
		Application Number	16/791,004
		Filing Date	2/14/2020
		First Named Inventor	Thomas BOYAJIAN
		Art Unit	3792
Examiner Name	MARLEN, TAMMIE K		
Attorney Docket Number	067286-0410		
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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 ⁶
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Attorney Docket No: 067286-0410

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				Filing Date		2/14/2020
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				Art Unit		3792
				Examiner Name		Tammie K. MARLEN
Sheet	1	of	1	Attorney Docket Number		067286-0410

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)			
	N1	5,211,938	05-18-1993	KENNEDY ET AL.	
	N2	5,211,938-B1	07-08-1997	KENNEDY ET AL.	
	N3	6,559,183-B1	05-06-2003	SCHMID ET AL.	
	N4	2016/0030565-A1	02-04-2016	WULF ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
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FOREIGN PATENT DOCUMENTS						
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		Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
	N5	JP-2002-529495-A	09-10-2002	ASAT AG APPLIED SCIENCE & TECHNOLOGY		ABS, =N3
	N6	JP-2010-515714-A	05-13-2010	PHOTOCURE ASA		ABS, =N4
	N7	JP-H04-500770-A	02-13-1992	QUEENS UNIVERSITY		√, = N1, N2

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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 ⁶
	N8	Japanese Office Action and English Translation, Application No. JP 2020-503004, Dated 8/2/2022 (6 pages)	√

Examiner Signature		Date Considered	
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< 2 of 2 Display >

JP,2010-515714,A

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Bibliography

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4C206ZB32

4C206ZB33

4C206ZB35

Overview

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(57) [Overview]

The invention provides the use of a photosensitizer which is a derivative of 5-aminolevulinic acid (5 - ALA) or 5 - ALA, or a salt thereof which can be used as a medicament in the manufacture of a composition for photodynamic therapy (PDT) for an animal. The PDT comprises (a), (b) : (a) administering a composition comprising the photosensitizer to an animal ; and (b) photoactivating the photosensitizer and using 1 or more of (I) - (iv). Or [that the side effects (for example, hurting and/or erythema) by the PDT are suppressed] -- or : (i) which can be softened -- the constituent contains the photosensitizer at less than (for example, 0.5 to 8 % by weight) 10% by weight of concentration -- (ii) Less than [of the photoactivation / front 2 hours] (for example, for 30 to 90 minutes) is medicated with the constituent, (iii) the photoactiv



tion is performed using a light source having a fluence rate of less than 50 mW / cm² (5-40 mW/cm²), and (iv) the photoactivity is performed using the converted sunlight ;. Preferably, side effects due to PDT are suppressed or alleviated by using (iii) or (iv) and (I) and / or (ii) in combination.

[Selected drawing] Nothing

Scope of Claims

Open



Detailed Description

Open



Written amendment

Open



Search Report

Open



2

of 2

Display



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			ガウスタッドヴェイエン 77
		最終頁に続く	

(54) 【発明の名称】 アミノレブリン酸およびその誘導体の使用

(57) 【要約】

本発明は、動物に対する光線力学的療法 (PDT) に用いる組成物の製造における、5-アミノレブリン酸 (5-ALA) もしくは5-ALAの誘導体 (例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用を提供するものであって、該PDTは (a), (b) を含み: (a) 該光増感剤を含む組成物を該動物に投与すること; および (b) 該光増感剤を光活性化すること、そして (i) ~ (iv) の1以上を用いることによって、該PDTによる副作用 (例えば、痛みおよび/または紅斑) が抑えられるかまたは和らげられる: (i) 該組成物が10重量%未満 (例えば、0.5~8重量%) の濃度で該光増感剤を含むこと、(ii) 該組成物が該光活性化の前2時間未満 (例えば、30~90分間) に投与されること、(iii) 該光活性化がフルエンス率50mW/cm²未満 (5~40mW/cm²) の光源を用いて行われること、(iv) 該光活性化が太陽光を用いて行われること。好ましくは、PDTによる副作用は、(iii) または (iv) と、(i) および/または (ii) とを組み合わせるによって抑えられるかまたは和らげられる。

【選択図】 なし

【特許請求の範囲】

【請求項1】

動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)もしくは5-ALAの誘導体(例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み：

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii)あるいは(iv)と、(i)および/または(ii)とを組み合わせる用いることによって、該PDTによる副作用(例えば、痛みおよび/または紅斑)を抑えるかあるいは少なくする：

(i) 該組成物が、10重量%未満(例えば、0.5~8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化の前2時間未満(例えば、5~90分間、好ましくは30~90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²(例えば、5~40mW/cm²)未満の光源を用いて行われること、

(iv) 該光活性化が、太陽光を用いて行われることを特徴とする使用。

【請求項2】

上記PDTが、その対応する標準的なPDT治療と治療効果が実質的に同じである請求項1に記載の使用。

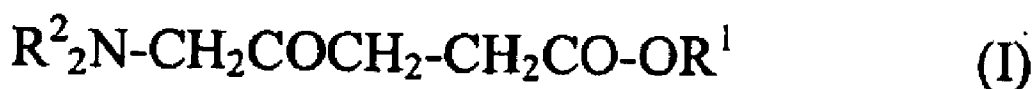
【請求項3】

上記光増感剤が、インビボでプロトポルフィリンIX(PPIX)または任意の他の光増感剤(例えば、PPIX誘導体)を形成できる5-ALAの誘導体である請求項1または2に記載の使用。

【請求項4】

上記光増感剤が、一般式Iの化合物：

【化1】



(式中、

R¹は、置換もしくは非置換の、直鎖状、分岐状または環状のアルキル基を表し；

R²は、それぞれ独立して、水素原子または任意に置換されたアルキル基、例えばR¹の基を表す。)または薬剤として使用し得るその塩である請求項1に記載の使用。

【請求項5】

式Iにおいて、R²それぞれが、水素原子を表す請求項4に記載の使用。

【請求項6】

式Iにおいて、R¹が、非置換アルキル基(好ましくはC₁₋₈アルキル、例えばC₁₋₆アルキル)またはアリール基によって置換されたアルキル基(例えばC₁₋₂アルキル、特にC₁アルキル)を表す請求項4または5に記載の使用。

【請求項7】

式Iにおいて、R¹が、アリール基によって任意に置換されたC₁₋₂アルキル基(好ましくはC₁アルキル基)基を表す請求項4または5に記載の使用。

【請求項8】

上記化合物が、メチルALAエステル、ベンジルALAエステルまたは置換されたベンジルALAエステルから選択される請求項7に記載の使用。

【請求項9】

式Iにおいて、 R^1 が、アリール基（例えば、フェニル）によって置換されたアルキル基（例えば、 C_{1-2} アルキル、特に C_1 ）を表す請求項4～6のいずれかに記載の使用。

【請求項10】

式Iにおいて、 R^1 が、アリールで置換された C_{1-4} アルキル基（好ましくは C_{1-2} アルキル、例えば C_1 アルキル）であり、好ましくは該アリール基は炭素原子を20個まで（例えば、炭素原子を12個まで）含み、該アリール基自体は置換されていてもよく、 R^2 それぞれが、請求項4で定義されたもの（例えば、 R^2 それぞれが水素）である請求項4～6のいずれかに記載の使用。

【請求項11】

上記化合物が、ベンジルALAエステルまたは置換されたベンジルALAエステル（例えば、4-ニトロベンジルALAエステルまたは4-クロロベンジルALAエステル）から選択される請求項10に記載の使用。

【請求項12】

式Iにおいて、 R^1 が、非置換アルキル基（好ましくは C_{1-8} アルキル、例えば C_{1-6} アルキル）を表す請求項4～6のいずれかに記載の使用。

【請求項13】

上記化合物が、メチルALAエステル、エチルALAエステル、プロピルALAエステル、ブチルALAエステル、ペンチルALAエステル、ヘキシルALAエステル、オクチルALAエステル、2-メチルペンチルALAエステル、4-メチルペンチルALAエステル、1-エチルブチルALAエステル、3,3-ジメチル-1-ブチルALAエステルから選択される請求項12に記載の使用。

【請求項14】

上記化合物が、メチルALAエステル、ヘキシルALAエステルおよび4-メチルペンチルALAエステル（好ましくは、メチルALAエステル）から選択される請求項12に記載の使用。

【請求項15】

さらに上記組成物が、第二の光増感剤を含む上記請求項のいずれかに記載の使用。

【請求項16】

上記組成物が、1～8重量%の濃度で、例えば2～4重量%の濃度で、5-ALAの誘導体である上記光増感剤を含む上記請求項のいずれかに記載の使用。

【請求項17】

PDTによる副作用が、上記光活性化の前5～60分間（例えば、20～40分間）の間に上記組成物を投与することによって抑えられるかまたは和らげられる上記請求項のいずれかに記載の使用。

【請求項18】

PDTによる副作用が、フルエンス率5～40mW/cm²、好ましくは10～35mW/cm²の光源を用いて光活性化することによって抑えられるかまたは和らげられる上記請求項のいずれかに記載の使用。

【請求項19】

PDTによる副作用が、(iii)と、(i)および/または(ii)とを組み合わせることで用いることによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項20】

PDTによる副作用が、(iii)および(i)を用いることによって、または(ii)および(ii)を用いることによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項21】

PDTによる副作用が、(iii)と、(i)および(ii)とを組み合わせることで用いることによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項22】

PDTによる副作用が、(iv)と、(i)および/または(ii)とを組み合わせるによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項23】

PDTによる副作用が、(iv)および(i)を用いることによって、または(iv)および(ii)を用いることによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項24】

PDTによる副作用が、(iv)と、(i)および(ii)とを組み合わせるによって抑えられるかまたは和らげられる請求項1～18のいずれかに記載の使用。

【請求項25】

上記PDTが、癌(例えば、基底細胞癌(bcc)、腫瘍、扁平上皮癌(scc)、ボ一エン病)、皮膚疾患(例えば、乾癬、光線性角化症および座瘡)ならびに感染(例えば、細菌感染、ウイルス感染または真菌感染、例えばヘルペスウイルス感染)に対する治療である上記請求項のいずれかに記載の使用。

【請求項26】

上記PDTが、座瘡に対する治療である請求項25に記載の使用。

【請求項27】

上記PDTが、座瘡以外の疾患(例えば、癌)に対する治療である請求項1～25のいずれかに記載の使用。

【請求項28】

上記PDTが、顔、頭皮または首の疾患に対する治療である上記請求項のいずれかに記載の使用。

【請求項29】

動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法であって、該PDTは(a)、(b)を含み：

(a) 請求項1～16のいずれかに定義した光増感剤を含む組成物を動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii)あるいは(iv)と、(i)および/または(ii)とを組み合わせるによって、該PDTによる副作用が抑えられるかあるいは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²未満(例えば、5～40mW/cm²)の光源を用いて行われること、

(iv) 該光活性化が、太陽光により実施されることを特徴とする方法。

【請求項30】

動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法で使用する製品またはキットであって、(a)、(b)を含む：

(a) 請求項1～16のいずれかに定義した組成物を有する容器、および

(b) 請求項1, 17～24のいずれかに定義した該PDTを実施するための使用説明書

ことを特徴とする製品またはキット。

【請求項31】

請求項1～15のいずれかに定義した光増感剤、および薬剤として使用し得る担体、希釈剤または賦形剤を含む医薬組成物であって、該光増感剤の濃度が、2～8重量%(例え

ば、2～4、5重量%)であることを特徴とする医薬組成物。

【請求項32】

治療(例えば、PDT)で用いる請求項31に記載の組成物。

【請求項33】

請求項1、17～28のいずれかに定義した光線力学的療法(PDT)の方法で使用する請求項1～16のいずれかに記載の組成物。

【請求項34】

動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)または5-ALAの誘導体(例えば、エステル)、もしくは薬剤として使用し得るこれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み：

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(i)～(iv)のうち1以上を用いることによって、該PDTの副作用(例えば、痛みおよび／または紅斑)が抑えられるかまたは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²未満(例えば、5～40mW/cm²)の光源を用いて行われること、

(iv) 該光活性化が、太陽光を用いて行われること

を特徴とする使用。

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、光線力学的療法(PDT)に関する。本発明は、特にPDTにおける5-アミノレブリン酸(5-ALA)および5-ALAの誘導体の使用に関し、本発明に係るPDTによると、PDTに起因する副作用(例えば、痛みおよび／または紅斑)が抑えられるかまたは和らげられる。

【背景技術】

【0002】

PDTは、光化学治療としても知られ、肌や他の上皮系組織もしくは粘膜に関するさまざまな異常または疾患、特に癌または前癌病変、および良性の病変(例えば、乾癬、光線性角化症(AK)、座瘡などの皮膚疾患)を治療するための技術である。PDTは、体の病変部への光感作薬(光化学治療剤)の塗布、それに続く、該光感作薬を活性化し細胞毒性を有する形態に変換するために光活性化する光線の照射を含み、これによって病的細胞が死滅するか、または該細胞の増殖ポテンシャルが減退する。

【0003】

さまざまな種類の光感作薬が知られており、ソラーレン、ボルフィリン(例えば、フォトフリン(登録商標))、クロリンおよびフタロシアニンが挙げられる。しかしながら、そのなかで5-アミノレブリン酸およびその誘導体(例えば、5-ALAエステルなどのエステル)は、当該分野において知られている臨床的にもっとも有用な光感作薬である。

【0004】

5-ALAおよび5-ALA誘導体を用いるPDTは、広範囲な疾病に対する治療において臨床的に有用であるが、このような治療の主な欠点は、とりわけ治療部位における副作用である。このような副作用としては、多くの場合、痛み、紅斑、腫れ、浮腫、火傷、痒み、剥離、高色素沈着ならびに長期にわたる炎症および治療後の過敏症が挙げられる。治療部位が顔、頭皮または首である場合、該副作用は特に望ましくない。この副作用は、

PDTが病変(例えば、座瘡、基底細胞癌、光線性角化症、扁平上皮癌)の治療である場合に頻繁に見られる。

【0005】

このような副作用が起こることは、座瘡を治療するPDTにおいて5-ALAエステルの使用を開示する国際公開第2006/051269号パンフレット[特許文献1]で認識されている。特許文献1には、16重量%のメチルALAエステルを含むクリームを被験者の顔に塗布し、その3時間後に非干渉性赤色光(光線量は 37 J cm^{-2})を被験者の顔に照射したという研究が記載されている。このとき、この治療は2週間後に再度行われた。この結果はメチルALAエステルを用いたPDTが座瘡の治療において有効であることを裏付けたものの、被験者はこの治療による痛みを指摘した。

【0006】

国際公開第02/13788号パンフレット[特許文献2]は、座瘡の治療をするPDTにおいて、ALAという酸を用いる同様の研究を開示している。このケースでは、20%のALAを被験者の背中に塗布して3時間後に、 150 J cm^{-2} の広帯域の光を被験者に照射した。このケースも先のケースと同様に、得られた結果がALAを用いるPDTが座瘡の治療に有効であることを裏付けたものの、被験者は過度の不快な副作用について報告している。例えば、特許文献2には、PDT治療の後、紅斑、高色素沈着および剥離が頻繁に見られることが報告され、またいくつかのケースにおいて、次の治療を延期せざるを得ないことが述べられている。治療中および治療後の痛み、火傷ならびに痒みの報告もまたよく見受けられた。

【0007】

特許文献2には上記治療方法が「高投与量、高エネルギー」の方法として記載されており、これによって座瘡の永続的な改善がなされるという。特許文献2には、座瘡の軽減を提供するよう考案された「低投与量、低エネルギー」の方法についても記載されている。この治療では0.1~10重量%のALAを塗布し、該ALAが皮膚に浸透するまで待ち、続いて $1\sim20\text{ J cm}^{-2}$ の光線量で照射する。特許文献2には、この方法は座瘡を軽減するために不定期な複数回の治療で用い、座瘡の軽減を維持するため必要に応じて行われることを提案している。このような方法が無痛であることは認識されているが、この治療方法の治療効果は、特許文献2に記載・実証されている高投与量、高エネルギーの方法の治療効果に及ばないことを、特許文献2は暗示している。

【手続補正書】

【提出日】平成20年12月1日(2008.12.1)

【手続補正1】

【補正対象書類名】特許請求の範囲

【補正対象項目名】全文

【補正方法】変更

【補正の内容】

【特許請求の範囲】

【請求項1】

動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)もしくは5-ALAの誘導体(例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み、

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iv)と、(i)および/または(ii)とを組み合わせ用いることによって、該PDTによる副作用(例えば、痛みおよび/または紅斑)を抑えるかあるいは少なくする：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化の前2時間未満(例えば、5～90分間、好ましくは30～90分間)に投与されること、

(iv) 該光活性化が、太陽光を用いて行われること

を特徴とする使用。

【請求項2】

癌を治療するための動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)もしくは5-ALAの誘導体(例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み：

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii)と、(i)および/または(ii)とを組み合わせ用いることによって、該PDTによる副作用(例えば、痛みおよび/または紅斑)を抑えるかあるいは少なくする：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化の前2時間未満(例えば、5～90分間、好ましくは30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²(例えば、5～40mW/cm²)未満の光源を用いて行われること

を特徴とする使用。

【請求項3】

上記PDTが、その対応する標準的なPDT治療と治療効果が実質的に同じである請求項1または2に記載の使用。

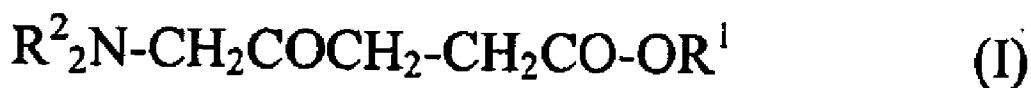
【請求項4】

上記光増感剤が、インビボでプロトポルフィリンIX(PpIX)または任意の他の光増感剤(例えば、PpIX誘導体)を形成できる5-ALAの誘導体である請求項1～3のいずれかに記載の使用。

【請求項5】

上記光増感剤が、一般式Iの化合物：

【化1】



（式中、

R¹は、置換もしくは非置換の、直鎖状、分岐状または環状のアルキル基を表し；R²は、それぞれ独立して、水素原子または任意に置換されたアルキル基、例えばR¹の基を表す。）または薬剤として使用し得るその塩である請求項1または2に記載の使用。

【請求項6】

式Iにおいて、R²それぞれが、水素原子を表す請求項5に記載の使用。

【請求項7】

式Iにおいて、R¹が、非置換アルキル基（好ましくはC₁₋₈アルキル、例えばC₁₋₆アルキル）またはアリール基によって置換されたアルキル基（例えばC₁₋₂アルキル、特にC₁アルキル）を表す請求項5または6に記載の使用。

【請求項8】

式Iにおいて、R¹が、アリール基によって任意に置換されたC₁₋₂アルキル基（好ましくはC₁アルキル基）基を表す請求項5または6に記載の使用。

【請求項9】

上記化合物が、メチルALAエステル、ベンジルALAエステルまたは置換されたベンジルALAエステルから選択される請求項8に記載の使用。

【請求項10】

式Iにおいて、R¹が、アリール基（例えば、フェニル）によって置換されたアルキル基（例えば、C₁₋₂アルキル、特にC₁）を表す請求項5～7のいずれかに記載の使用。

【請求項11】

式Iにおいて、R¹が、アリールで置換されたC₁₋₄アルキル基（好ましくはC₁₋₂アルキル、例えばC₁アルキル）であり、好ましくは該アリール基は炭素原子を20個まで（例えば、炭素原子を12個まで）含み、該アリール基自体が置換されていてもよく、

R²それぞれが、請求項5で定義されたもの（例えば、R²それぞれが水素）である請求項5～7のいずれかに記載の使用。

【請求項12】

上記化合物が、ベンジルALAエステルまたは置換されたベンジルALAエステル（例えば、4-ニトロベンジルALAエステルまたは4-クロロベンジルALAエステル）から選択される請求項11に記載の使用。

【請求項13】

式Iにおいて、R¹が、非置換アルキル基（好ましくはC₁₋₈アルキル、例えばC₁₋₆アルキル）を表す請求項5～7のいずれかに記載の使用。

【請求項14】

上記化合物が、メチルALAエステル、エチルALAエステル、プロピルALAエステル、ブチルALAエステル、ペンチルALAエステル、ヘキシルALAエステル、オクチルALAエステル、2-メチルペンチルALAエステル、4-メチルペンチルALAエステル、1-エチルブチルALAエステル、3,3-ジメチル-1-ブチルALAエステルから選択される請求項13に記載の使用。

【請求項15】

上記化合物が、メチルALAエステル、ヘキシルALAエステルおよび4-メチルペンチルALAエステル（好ましくは、メチルALAエステル）から選択される請求項13に記載の使用。

【請求項16】

さらに上記組成物が、第二の光増感剤を含む上記請求項のいずれかに記載の使用。

【請求項17】

上記組成物が、1～8重量%の濃度で、例えば2～4重量%の濃度で、5-ALAの誘導体である上記光増感剤を含む上記請求項のいずれかに記載の使用。

【請求項18】

PDTによる副作用が、上記光活性化の前5～60分間（例えば、20～40分間）の間に上記組成物を投与することによって抑えられるかまたは和らげられる上記請求項のいずれかに記載の使用。

【請求項19】

PDTによる副作用が、フルエンス率5～40mW/cm²、好ましくは10～35mW/cm²の光源を用いて光活性化することによって抑えられるかまたは和らげられる上記請求項のいずれかに記載の使用。

【請求項20】

PDTによる副作用が、(iii)および(i)を用いることによって、または(ii)および(ii)を用いることによって抑えられるかまたは和らげられる請求項2～19のいずれかに記載の使用。

【請求項21】

PDTによる副作用が、(iii)と、(i)および(ii)とを組み合わせる用いることによって抑えられるかまたは和らげられる請求項2～19のいずれかに記載の使用。

【請求項22】

PDTによる副作用が、(iv)および(i)を用いることによって、または(iv)および(ii)を用いることによって抑えられるかまたは和らげられる請求項1および3～19のいずれかに記載の使用。

【請求項23】

PDTによる副作用が、(iv)と、(i)および(ii)とを組み合わせる用いることによって抑えられるかまたは和らげられる請求項1および3～19のいずれかに記載の使用。

【請求項24】

上記PDTが、癌（例えば、基底細胞癌(bcc)、腫瘍、扁平上皮癌(scc)、ボエーン病）、皮膚疾患（例えば、乾癬、光線性角化症および座瘡）ならびに感染（例えば

、細菌感染、ウイルス感染または真菌感染、例えばヘルペスウイルス感染)に対する治療である請求項1および3～23のいずれかに記載の使用。

【請求項25】

上記PDTが、座瘡に対する治療である請求項24に記載の使用。

【請求項26】

上記PDTが、座瘡以外の疾患(例えば、癌)に対する治療である請求項1および3～24のいずれかに記載の使用。

【請求項27】

上記PDTが、顔、頭皮または首の疾患に対する治療である上記請求項のいずれかに記載の使用。

【請求項28】

動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法であって、該PDTは(a)、(b)を含み：

(a) 請求項1および3～17のいずれかに定義した光増感剤を含む組成物を動物に投与すること；および

(b) 該光増感剤を光活性化すること、

そして、(iv)と、(i)および/または(ii)とを組み合わせる用いることによって、該PDTによる副作用を抑えられるかあるいは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iv) 該光活性化が、太陽光により実施されること

を特徴とする方法。

【請求項29】

癌を治療するための動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法であって、該PDTは(a)、(b)を含み：

(a) 請求項2～17のいずれかに定義した光増感剤を含む組成物を動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii)と、(i)および/または(ii)とを組み合わせる用いることによって、該PDTによる副作用を抑えられるかあるいは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²未満(例えば、5～40mW/cm²)の光源を用いて行われること

を特徴とする方法。

【請求項30】

動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法で使用する製品またはキットであって、(a)、(b)を含む：

(a) 請求項1～17のいずれかに定義した組成物を有する容器、および

(b) 請求項1、2および18～23のいずれかに定義した該PDTを実施するための使用説明書

ことを特徴とする製品またはキット。

【請求項31】

請求項1、2および18～27のいずれかに定義した光線力学的療法(PDT)の方法

で使用する請求項 1 ～ 1 7 のいずれかに記載の組成物。

【手続補正書】

【提出日】平成21年9月25日(2009.9.25)

【手続補正1】

【補正対象書類名】特許請求の範囲

【補正対象項目名】全文

【補正方法】変更

【補正の内容】

【特許請求の範囲】

【請求項1】

動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)もしくは5-ALAの誘導体(例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み：

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iv) と、(i) および／または(ii) とを組み合わせる用いることによって、該PDTによる副作用(例えば、痛みおよび／または紅斑)を抑えるかあるいは少なくする：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化の前2時間未満(例えば、5～90分間、好ましくは30～90分間)に投与されること、

(iv) 該光活性化が、太陽光を用いて行われること

を特徴とする使用。

【請求項2】

癌を治療するための動物に対する光線力学的療法(PDT)に用いる組成物の製造における、5-アミノレブリン酸(5-ALA)もしくは5-ALAの誘導体(例えば、エステル)、またはその薬剤として使用し得るそれらの塩である光増感剤の使用であって、該PDTは(a)、(b)を含み：

(a) 該光増感剤を含む組成物を該動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii) と、(i) および／または(ii) とを組み合わせる用いることによって、該PDTによる副作用(例えば、痛みおよび／または紅斑)を抑えるかあるいは少なくする：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化の前2時間未満(例えば、5～90分間、好ましくは30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²(例えば、5～40mW/cm²)未満の光源を用いて行われること

を特徴とする使用。

【請求項3】

上記PDTが、その対応する標準的なPDT治療と治療効果が実質的に同じである請求項1または2に記載の使用。

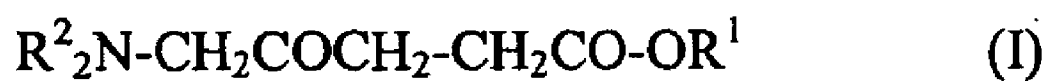
【請求項4】

上記光増感剤が、インビボでプロトポルフィリンIX(PpIX)または任意の他の光増感剤(例えば、PpIX誘導体)を形成できる5-ALAの誘導体である請求項1～3のいずれかに記載の使用。

【請求項5】

上記光増感剤が、一般式Iの化合物：

【化1】



(式中、

R^1 は、置換もしくは非置換の、直鎖状、分岐状または環状のアルキル基を表し；

R^2 は、それぞれ独立して、水素原子または任意に置換されたアルキル基、例えば R^1 の基を表す。)または薬剤として使用し得るその塩である請求項1または2に記載の使用。

【請求項6】

式Iにおいて、 R^2 それぞれが、水素原子を表す請求項5に記載の使用。

【請求項7】

式Iにおいて、 R^1 が、非置換アルキル基(好ましくは C_{1-8} アルキル、例えば C_{1-6} アルキル)またはアリール基によって置換されたアルキル基(例えば C_{1-2} アルキル、特に C_1 アルキル)を表す請求項5または6に記載の使用。

【請求項8】

さらに上記組成物が、第二の光増感剤を含む上記請求項のいずれかに記載の使用。

【請求項9】

PDTによる副作用が、上記光活性化の前5～60分間(例えば、20～40分間)の間に上記組成物を投与することによって抑えられるかまたは和らげられる上記請求項のいずれかに記載の使用。

【請求項10】

上記PDTが、癌(例えば、基底細胞癌(bcc)、腫瘍、扁平上皮癌(scc)、ボアエン病)、皮膚疾患(例えば、乾癬、光線性角化症および座瘡)ならびに感染(例えば、細菌感染、ウイルス感染または真菌感染、例えばヘルペスウイルス感染)に対する治療である請求項1および3～9のいずれかに記載の使用。

【請求項11】

動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法であって、該PDTは(a)、(b)を含み：

(a) 請求項1および3～8のいずれかに定義した光増感剤を含む組成物を動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iv)と、(i)および/または(ii)とを組み合わせる用いることによって、該PDTによる副作用が抑えられるかあるいは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iv) 該光活性化が、太陽光により実施されること
を特徴とする方法。

【請求項12】

癌を治療するための動物の光線力学的療法(PDT)による副作用(例えば、痛みおよび/または紅斑)を抑えられるかまたは和らげられる方法であって、該PDTは(a)、

(b)を含み：

(a) 請求項2～8のいずれかに定義した光増感剤を含む組成物を動物に投与すること；および

(b) 該光増感剤を光活性化すること、

(iii)と、(i)および/または(ii)とを組み合わせる用いることによって、該PDTによる副作用が抑えられるかあるいは和らげられる：

(i) 該組成物が、10重量%未満(例えば、0.5～8重量%)の濃度で該光増感剤を含むこと、

(ii) 該組成物が、該光活性化する前2時間未満(例えば、30～90分間)に投与されること、

(iii) 該光活性化が、フルエンス率が50mW/cm²未満(例えば、5～40mW/cm²)の光源を用いて行われること

を特徴とする方法。

【請求項13】

動物の光線力学的療法（PDT）による副作用（例えば、痛みおよび／または紅斑）を抑えられるかまたは和らげられる方法で使用する製品またはキットであって、（a）、（b）を含む：

（a）請求項1～8のいずれかに定義した組成物を有する容器、および

（b）請求項1，2および9のいずれかに定義した該PDTを実施するための使用説明書

ことを特徴とする製品またはキット。

【請求項14】

請求項1，2，9および10のいずれかに定義した光線力学的療法（PDT）の方法で使用する請求項1～8のいずれかに記載の組成物。

【国際調査報告】

【化1】

INTERNATIONAL SEARCH REPORT		International application No. PCT/GB2008/000086
A. CLASSIFICATION OF SUBJECT MATTER INV. A61K31/221 A61K41/00 A61K31/197 A61P17/10 A61P35/00		
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) A61K A61P		
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) EPO-Internal, CHEM ABS Data, EMBASE, BIOSIS, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
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☒ 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 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. "B" document member of the same patent family		
Date of the actual completion of the international search 24 June 2008		Date of mailing of the international search report 09/07/2008
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentstein 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx. 31 651 epo nl Fax: (+31-70) 340-3016		Authorized officer Jakobs, Andreas

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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INTERNATIONAL SEARCH REPORT	International application No. PCT/GB2008/000086
Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)	
<p>This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:</p> <p>1. ☒ Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claim 29 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.</p> <p>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:</p> <p>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).</p>	
Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)	
<p>This International Searching Authority found multiple inventions in this international application, as follows:</p> <p>1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.</p> <p>2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.</p> <p>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.:</p> <p>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.:</p> <p>Remark on Protest</p> <p>☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.</p> <p>☐ 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.</p> <p>☐ No protest accompanied the payment of additional search fees.</p>	

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(51)Int.Cl.	F I		テーマコード (参考)
A 6 1 P 31/10 (2006.01)	A 6 1 P	31/10	
A 6 1 P 31/12 (2006.01)	A 6 1 P	31/12	
A 6 1 P 31/22 (2006.01)	A 6 1 P	31/22	
A 6 1 P 17/02 (2006.01)	A 6 1 P	17/02	

(81)指定国 AP(BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), EA(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), EP(AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, T R), OA(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG), AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, 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, IS, JP, KE, K G, KM, 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, PG, PH, PL, PT , RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

(72)発明者 クラベネス, ジョー

ノルウェー オスロ エヌー１１６６, ミッドタセン ５

Fターム(参考) 4C206 AA01 AA02 DB03 DB43 MA01 MA04 NA14 ZA89 ZB26 ZB32
ZB33 ZB35

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JP,04-500770,A(1992)

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Overview

Close



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Scope of Claims

Close

[Patent Claims]

Patient's skin ; conjunctiva ; respiratory, digestive and vaginal mucosa ; endometrium ; and urinary tract ; 1.

A method for treating malignant and non-malignant tissue in a cell layer comprising :
5-aminolevulinic acid for inducing the synthesis of protoporphyrin IX

An effective amount of an effective amount of a compound of formula I is administered to said patient and photoactivated of said protoporphyrin IX.

A method comprising exposing said lesion to light in a spectrum for use.

2. the Aforementioned Malignancy -- from Basal Cell Carcinoma, Basosquamous Carcinoma, and Squamous Cell Carcinoma -- Selection

The method of claim 1, wherein the method is performed.

3. The Aforementioned Non-Malignancy is Description to Claim 1 Chosen from Psoriasis and Reproductive Organ **.

Method.

4. It is Note to Claim 1 Which is Thing in Region whose Aforementioned Photoactivation Light is 350 to 635 Nm.

The method of *.

5. a method of treating menorrhagia, wherein a 5-aminolevulinic acid is localized to an endometrium ;

It has been administered and has wavelengths within the spectrum of photoactivation of protoporphyrin IX.

A method comprising exposing the endometrium to light.

The method of claim 1, wherein said 5 - aminolevulinic acid is administered parenterally. 6.

The method of claim 1, wherein said 5 - aminolevulinic acid is administered topically. 7.

The method of claim 1, wherein said 5 - aminolevulinic acid is administered orally. 8.

Malignant and non-malignant growth of the patient's skin, mucosa, endometrium and urinary cell layer 9.

It is [in / are a treating method of *** and / the aforementioned lesion] a synthesis of protoporphyrin IX.

Effective amounts of precursors of protoporphyrin IX in the biosynthetic pathway of heme for



duction

The aforementioned patient is medicated and it is photoactivation working effect *** of aforementioned protoporphyrin IX.

A method comprising exposing the lesion to light in a torsin.

The method of claim 9, wherein said precursor is a 5-aminolevulinic acid . 10.

Malignant and non-malignant abnormalities of the skin, mucous membranes, endometrium and urinary cell layers of patients, 11.

In a method of detecting a lesion, the method comprises the steps of : ****

***** in the biosynthetic pathway of heme to induce synthesis of filagyrin IX

An effective amount of a precursor of IX is administered to said patient to adsorb said protoporphyrin IX.

Exposing the patient to light having a wavelength within the spectrum, thereby inducing fluorescence.

How to carry out and include detecting the aforementioned fluorescence.

Detailed Description

Close

[Detailed description of the invention]

Method for the detection and treatment of malignant and non-malignant lesions by photochemotherapy

The field of invention

The present invention relates to the detection and treatment of certain tissue abnormalities (both cancerous and non-malignant) by inductive fluorescence and photochemotherapy, respectively.

The background of invention

Normally, tissue abnormalities affecting the skin are detected and evaluated by a combination of visual inspection and palpation. In certain clinical situations, the sensitivity of the visual inspection can be increased by the use of non-white light (either ultraviolet or visible narrow band) or by prior application of contrasting agents such as dilute acetic acid or certain dyes. Tissue abnormalities including non-palpable surfaces (e.g., bronchi or bladders) can be visualized by an appropriate scope. Some specialized scopes are capable of detecting stimulated fluorescence. If an anomaly in question is related to any difference in the extent or pattern of vascularization of the tissue, then such a scope may be used to determine the limit of an abnormally involved region by visualizing the injected fluorescent agent when it is passed through the vasculature of both diseased and nearby normal tissues.



In addition, the fluorescence detection scope has been used experimentally to identify areas of tissue that exhibit strong porphyrin fluorescence following intravenous injection of exogenous porphyrins, such as hematoporphyrin IX (HpIX), hematoporphyrin derivatives (HpIX), or "diethyl hematoporphyrin Ether" (photofrin II). Such porphyrins tend to accumulate predominantly in malignant tissue, but they accumulate in the tissue or in the rapidly growing tissue of the embryo or fetus that is regenerating after injury. Normal liver, spleen and kidney also tend to accumulate their porphyrins. Using such a compound and fluorescence detection scope, regions of malignant tissue that are too small to be identified by standard form of appearance inspection have been identified in the bronchi and bladder.

Unfortunately, a clinically significant (photosensitized) amount of porphyrin remains in the skin for at least 2 weeks (optionally more than 2 months) after intravenous injection of HpIX, hP D or photofrin II. This means that the patient must avoid exposure to sunlight (direct or sunlight through the window pane) for an extended period of time after injection. As can be appreciated, patient compliance (compliance) often becomes poor and a "sunburn" of accidental phototoxicity generally occurs for weeks after diagnosis or therapeutic injection of porphyrins. Persistent photosensitization is a major hazard associated with this method and is why it is not widely utilized.

Standard or customary therapeutic forms of cancer are surgery, radiotherapy and chemotherapy. However, other modalities of therapy, including photochemotherapy or photodynamic therapy (PDT), are also known. PDT is currently used to treat some different types of cancer and certain non-malignant pathologies such as psoriasis based on experience. A patient is administered a photoactivatable reagent that has a degree of specificity for the tissue to be treated. The tissue region containing the target tissue is then exposed to photoactivated light which destroys the target tissue but only provides mild and reversible damage to other tissues in the same treatment region.

Currently, there are 2 main types of photochemotherapeutic agents for clinical use. The first type of methoxypsoralen is administered systemically. Ultraviolet light is essential to activate them. Local exposure of psoralen-containing tissue to ultraviolet light induces local photochemical reactions that covalently bind the drug to the DNA of viable cells and destroy their proliferative power. The 2 type of porphyrin is administered systemically (by intravenous injection), but sometimes is administered locally or by intralesional injection. They can be activated by visible (red) light. Local exposure of the porphyrin-containing tissue to such light does not induce a chemical reaction between the cellular component and the porphyrin molecule. Instead, the porphyrin acts as a catalyst by trapping the energy of the photoactivated light and then passing it to an oxygen molecule, which in turn turns it into an excited state capable of oxidizing the neighboring molecules or structures. Cell death is caused by damage to the essential membrane structure, rather than primarily caused by DNA damage.

Photochemotherapy is currently being used to treat non-malignant lesions, including certain types of cancer and psoriasis. Although the goal of such therapy is sometimes healing (primary



y for basal cell carcinoma), the goal is usually relaxation by local control when standard therapy forms probably will give the patient a significant degree of effect.

Methoxypsoralen (PUVA) therapy is used primarily for the treatment of psoriasis, but sometimes is also used to treat very superficial cancers (mainly mushroom-like mycoses). However, such treatment has 2 serious problems. First, this method has proven to be carcinogenic in humans. 2, the depth of depth that can kill malignant tissue is limited to a few millimeters below the irradiated surface, since light activated light is absorbed very strongly into most tissues. These problems severely limit the usefulness of methoxypsoralen for photochemotherapy.

Currently, porphyrins most commonly used for photochemotherapy are the hemi-purified forms of hematoporphyrin IX (HpIX), hematoporphyrin derivatives (hPD), and photofrin II (Photofrin II). When porphyrins are used as photosensitizing agents, cell death occurs due to damage of the essential membrane structure rather than DNA damage. Thus, malignant transformation is not a serious problem. Furthermore, the visible (red) light used to photoactivate the porphyrin penetrates tissue much deeper than the ultraviolet light used to photoactivate methoxypsoralen, so that the depth of the porphyrin treated tissue is much greater. It is sometimes possible to destroy malignant tissue without causing clinically significant damage to nearby normal tissues, since certain types of porphyrins exhibit a significant tendency to accumulate predominantly in malignant tissue.

It is ability.

A major problem with systemic application of HpIX, hPD and photofrin II is that a photosensitized concentration persists on the skin for several weeks to several months after their administration. As a result, serious, accidental phototoxic skin reactions may occur unless the patient avoids sunlight (either directly or through a window pane) until the concentration of photosensitizer in the skin decreases to a harmless level. Currently, the problem of photosensitization following administration of porphyrins has been addressed by advising any form of exposure to sunlight for at least 2 weeks of injection (or to very bright artificial light) and subsequently very carefully initiating exposure to sunlight. Since it is quite inconvenient to do this, not all patients follow their teachings. In addition, the use of sunscreens with high light shielding forces is inferred with an alert that only some risk is reduced and that it is not completely removed. In a few cases, a patient with photosensitization for more than 1 months after treatment was administered a high daily dose of β -carotene for several months in an attempt to prevent accidental phototoxic injury. Finally, attempts have been made to reduce phototoxicity by topically applying a photosensitizer to a limited area.

However, when HpIX or hPD is applied topically in DMSO (dimethylsulfoxide) Azone or some other vehicle for the purpose of increasing diffusion into tissue, another type of problem is encountered. When the DMSO Azone becomes diluted with normal tissue fluid to such an extent that the porphyrin is no longer able to diffuse into tissue (or remains in solution), it tends to become immobilized where it is present. As a result, topical application of porphyrins is associated



d with decreased specificity for malignant tissue and normal tissues near the site of application may produce persistent photosensitization from the local concentration of porphyrins.

The object of invention

It is an object of the present invention to provide a method for detecting certain types of malignant and non-malignant tissues by inductive luminescence.

It is a further object of the present invention to provide a method of photodynamic (photosensitization) treatment which can be administered either systemically or locally using an agent which is not itself a photosensitizer but which induces the synthesis of protoporphyrin IX (PpIX) in vivo.

The description of invention

According to one aspect of the invention, a method of detecting malignant and non-malignant lesions in a patient is provided which induces the accumulation of protoporphyrin IX in said lesion. A method is provided which comprises administering to said patient an effective amount of a precursor of protoporphyrin IX in the biosynthetic pathway of heme and exposing said lesion to light having a wavelength within the absorption spectrum of said protoporphyrin IX, thereby inducing fluorescence in said lesion.

According to another aspect of the invention, a method for treating malignant and non-malignant hyperproliferative lesions of the skin, mucosa, endometrium and urinary tract of a patient (urothelium) is provided which induces the synthesis of protoporphyrin IX in said lesion. A method is provided which comprises administering an effective amount of a precursor of a protoporphyrin IX in a biosynthetic pathway of heme to said patient, and exposing said lesion to light having a wavelength within the spectrum of photoactivation of said PpIX, thereby inducing fluorescence in said lesion.

In a preferred embodiment of the invention, the precursor of the preferred protoporphyrin IX is a 5-aminolevulinic acid known as a 5-amino-4-oxopentanoic acid and the preferred wavelength of the photoactivated light is in the region of 350 to 635 nm, more preferably about 635 nm.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Protoporphyrin IX (PpIX), a naturally occurring photosensitizer, is a precursor of heme in the heme biosynthetic pathway. Since heme is necessary for the synthesis of various important heme-containing enzymes, all nucleated cells have minimal ability to synthesize at least PpIX. Some types of cells and tissues can synthesize relatively large amounts of PpIX. Under normal conditions, the synthesis of PpIX in such tissues is under stringent feedback control such that the cells produce PpIX at a rate which is just 10 minutes to meet the requirements of heme. However, synthesis of 5-aminolevulinic acid (ALA), which is a normal rate-limiting step of this process, can be bypassed by the provision of exogenous ALA, porphobilinogen or other PpIX precursor. Certain tissues and organs will accumulate a large excess of PpIX so that they are fluorescent and photosensitized. At least in the case of skin, PpIX appears to be synthesized in situ. ALA, which is commercially available from Sigma Chemical Company and is water-soluble

can be administered orally, topically or by injection. An oral or parenteral route results in the induction of clinically useful concentrations of PpIX into certain benign and malignant tissues throughout the body. Since only one type of tissue can synthesize a clinically useful amount of PpIX when supplying an excess of ALA, the supply of ALA is advantageous only if the affected tissue is at a site where photoactivated light can reach. At present, treatment of basal cell carcinomas of the skin, mucosal (of the respiratory, digestive and vaginal), endometrium and urinary cell layers (urothelium), basal spinocellular carcinomas and spiny cell carcinomas and other lesions is expected. As sites: (i) the skin and conjunctiva; (ii) the inner layers of the mouth, pharynx, esophagus, stomach, intestine and intestine appendages, rectum and anal canal; (iii) the inner layer of the nasal tract, nasal cavity, nasopharynx, trachea, bronchi and bronchioli; (iv) the inner layer of the ureter, bladder, and urethra; and (v) the vagina. Inner layers of cervix and uterus; (vi) parietal pleura and lung pleura; (vii) inner layer of abdominal cavity and pelvic cavity; Mention may be made of lesions associated with the surface of the organs contained in the interior of the cavities; (viii) the dura and meningeal; (ix) any tumor in the solid tissue which can be rendered accessible to the photoactivated light either directly at the time of surgery, or by an optical fiber inserted through a needle.

While 1 to 10% of incident red light (600 to 700 nm) can pass through a human tissue slab having a thickness of 1 cm, blue light (about 400 nm) can pass through human tissue of the same thickness of only 0.001% or less.

As shown, the wavelength of the photoactivated light is somewhat important. Thus, if the photosensitizer absorbs red light strongly, it will be more successful. PpIX strongly absorbs red light. This approach has several advantages over the prior art. First, PpIX has a much shorter half-life than HpIX, hPD, or photofrin II in normal tissues. This greatly reduces the risk of accidental phototoxic skin reactions after treatment. Although the topical application of ALA to a certain type of lesion can derive PpIX to the second inside those lesions, it is not derived to it at other places. This improves the specificity of the treatment, reduces the accidental phototoxic response to only low levels, and greatly reduces the amount of both ALA and PpIX that would have been exposed systemically if a uniform effective amount of ALA is to be administered systemically. Both ALA and PpIX are common metabolites and are very easily processed by biochemical mechanisms in the body. However, since a very large amount of ALA (as well as a large amount of HpIX or hPD) is associated with a temporary decrease in kinetic neurotransmission rate, it is desirable to reduce the dose of ALA to a minimum amount that is still effective. Topical application requires much less ALA than systemic administration. 3, PpIX is rapidly deactivated by photoactivated light. After exposure of the PpIX containing tissue to the therapeutic dose of photoactivatable light, there is a substantial decrease in the photosensitization of the tissue within the treatment volume. As a result, if PpIX is induced by topical application of ALA to a particular lesion, the patient can be exposed to the sun immediately after treatment without the risk of serious phototoxicity. 4, when administered orally, topically or by injection, ALA

is an effective inducer of PpIX. In contrast, HpIX, hPD and photofrin II are most often effective only when administered by injection. This pluripotency of ALA increases accessibility to daily use by physicians. This is because oral and topical routes of administration are much more convenient than parenteral. 5, normal and abnormal tissues that can be sensitized by administration of ALA are somewhat different from those that can be sensitized by administration of HpIX, hPD, or photofrin II. Thus, ALA may be useful in clinical situations where other photosensitizing agents are not useful.

The technique of the present invention is not only an alternative method of implementing what can be performed, but is indeed a significant advance in therapeutic capacity.

Example 1

A 87 year old patient diagnosed with recurrent intraepithelial vestigious cell carcinoma of the right cheek and mandible was treated by topical application of ALA in 17% (w / w) Glaxal base at a dose of 100 mg ALA per lesion. After 2.5 hours of application, the lesions were exposed to light at a dose of 52.5 mW / cm² (intensity × time) to the output of a 500 watt tungsten lamp filtered to remove photoactivatable light, i. e., infrared (thermal filter) and a wavelength of 600 nm or less (Hoya R - 60 filter). Patients were assessed for 40 days after treatment and the lesions were judged to have responded completely.

Example 2

On top of the upper and outside of the right ear, a 73 year old patient diagnosed with intraepithelial vestigious carcinoma was treated by topical application of ALA in 10% (w / w) Glaxal base at a dose of 35 mg per lesion. 3 hours after application of ALA, lesions were exposed to 26 mW time / cm² light from the light source described in Example 1. Evaluation for 21 days after treatment showed a complete response.

Example 3

A 64 year old patient diagnosed as having multiple barbed cell carcinoma at the next site.

- (1) Back, left shoulder ;
- (2) Spine, right cage
- (3) The back, a right thorax lower part
- (4) The left-hand facies dorsalis scapulae, near finger
- (5) the dorsum of the left hand side, center portion ;
- (6) A left hand, near a thumb joint (about 10-mm upheaval)

Lesions 1,2 and 3 were treated with 20 mg ALA per 20%w/wGlaxal base lesion. After 3 hours, it was exposed to light activated light from the light source described in Example 1 at a dose of 50 mW hour / cm². 10 days after treatment, lesion 1 had almost complete response, lesion 2 had a partial response and lesion 3 had a complete response. Next, lesions 1 and 2 and lesions 4,5 and 6 are treated with 22 mg ALA in a 10%w/wGlaxal base for 3 hours, and the following dose :

Lesion 1-17 mW / cm²

Lesion 2-17 mW / cm²



Lesion 4-26 mW / cm²

Lesion 5-26 mW / cm²

Lesion 6-26 mW / cm²

In this case, the light was exposed to light. 25 days after treatment, patients were evaluated as follows :

Lesion 1 - Complete response

Lesion 2 - Complete response

Lesion 4 - Recurrence

Lesion 5 partial response

A drop of about 3 in 6-10 lesions.

Example 4

Patients at 43 years of age were diagnosed as having (1) spine, left shoulder and (2) back, high lumbar region, and right basal cell carcinoma, and that this patient was treated with 50 mg ALA per 33%w/w Glaxal base lesion for 3 hours. The lesion was then photoactivated at 37 mW time / cm² from the light source described in Example 1. Evaluation for 64 days after treatment showed a complete response of both lesions.

Example 5

ALA was dissolved in isotonic saline solution and then systemically administered to mice at a dose of 100 to 500 mg per 1 kg of body weight either subcutaneously or intraperitoneally. After 3 hours, mice were sacrificed and frozen sections of the uterus were taken. Examination of these sections by fluorescence microscopy showed that the endometrium showed strong protoporphyrin fluorescence, but no lower uterine myoma. Since ALA was administered systemically, it must be sure that it was present in the myometrial, and a subsequent deletion of protoporphyrin fluorescence in the myometrial would be when an excess of exogenous ALA was supplied.

It is surely *. Thus, when ALA is applied directly to the surface of the endometrium, the myometrial will not be sensitized and subsequent exposure of the endometrium and myometrial to photoactivated light will result in preferential ablation of endometrial tissue.



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⑮ 発明の名称 光化学療法による悪性および非悪性病変の検出および治療方法

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請求の範囲

1. 患者の皮膚; 結膜; 呼吸器、消化器および腫の粘膜; 子宮内膜; 並びに尿路細胞層の悪性および非悪性組織の異常および病変の治療方法であって、前記病変においてプロトポルフィリンIXの合成を誘導するために5-アミノレブリン酸の有効量を前記患者に投与し、そして前記プロトポルフィリンIXの光活性化作用スペクトル内の光に前記病変を暴露することを含んで成る方法。
2. 前記悪性病変が、基底細胞癌、基底有棘細胞癌および有棘細胞癌から選択される、請求項1に記載の方法。
3. 前記非悪性病変が乾癬および生殖器いぼから選択される、請求項1に記載の方法。
4. 前記光活性化光が 350-635nm の領域中のものである、請求項1に記載の方法。
5. 月経過多の治療方法であって、子宮内膜に5-アミノレブリン酸を局所的に投与し、そしてプロトポルフィリンIXの光活性化作用スペクトル内の波長を有する光に前記子宮内膜を暴露することを含んで成る方法。
6. 前記5-アミノレブリン酸が非経口投与される、請求項1に記載の方法。
7. 前記5-アミノレブリン酸が局所投与される、請求項1に記載の方法。
8. 前記5-アミノレブリン酸が経口投与される、請求項1に記載の方法。

9. 患者の皮膚、粘膜、子宮内膜および尿路細胞層の悪性および非悪性の増殖過剰病変の治療方法であって、前記病変においてプロトポルフィリンIXの合成を誘導するためにヘムの生合成経路中のプロトポルフィリンIXの前駆体の有効量を前記患者に投与し、そして前記プロトポルフィリンIXの光活性化作用スペクトル内の光に前記病変を暴露することを含んで成る方法。

10. 前記前駆体が5-アミノレブリン酸である、請求項9に記載の方法。

11. 患者の皮膚、粘膜、子宮内膜および尿路細胞層の悪性および非悪性の異常および病変の検出方法であって、前記異常および病変において優勢的にプロトポルフィリンIXの合成を誘導するためにヘムの生合成経路中のプロトポルフィリンIXの前駆体の有効量を前記患者に投与し、前記プロトポルフィリンIXの吸収スペクトル内の波長を有する光に前記患者を暴露し、それによって蛍光を誘導し、そして前記蛍光を検出することを含んで成る方法。

明 細 書

光化学療法による悪性および非悪性病変
の検出および治療方法

発明の分野

それぞれ誘導的蛍光および光化学療法による、或る種の組織異常（悪性および非悪性の両方）の検出および治療に関する。

発明の背景

通常は皮膚に影響を及ぼす組織異常は、外観検査と触診の組合せにより検出および評価される。或る臨床的状況では、非白色光（紫外光または可視中の狭いバンド）の使用により、または希酸酸もしくは或る種の染料といった対比強化剤の事前適用により、外観検査の感度を高めることができる。触診できない表面を含む組織異常（例えば気管支または膀胱）は、適当なスコープにより視覚化することができる。幾つかの特殊スコープは、誘導的蛍光を検出することができる。問題の異常が組織の血管形成の範囲またはパターンのいずれかの相違に関連するならば、そのようなスコープを用いて、それを病変組織と近隣の正常組織の両方の血管系に通過させた時に注入された蛍光薬剤を視覚化することにより、異常に関連する領域の限界を決定することができる。

加えて、蛍光検出スコープは、外因性ポルフィリン、例え

うな或る種の非悪性病変を治療するために現在使われている。患者は、処置すべき組織に対して或る程度の特異性を有する光活性化試薬を投与される。次いで標的組織を含む組織領域が、標的組織を破壊するが同じ処置領域中の他の組織に対しては緩和で且つ可逆的な損傷のみを生じるような光活性化光に暴露される。

現在、臨床用途の2つの主要タイプの光化学療法薬がある。第一のタイプであるメトキシソラレンは全身投与される。それらを活性化するために紫外光は不可欠である。紫外光へのソラレン含有組織の局所的暴露は、該薬剤を生存細胞のDNAに共有結合させ、それらの増殖力を破壊する局所的な光化学反応を誘導する。第二のタイプであるポルフィリンは、全身投与されるが（静注により）、時には局所的にまたは病変内注射のいずれかにより投与されることがある。それらは可視（赤色）光により活性化され得る。そのような光へのポルフィリン含有組織の局所的暴露は、細胞成分とポルフィリン分子との間の化学反応を誘導しない。その代わり、ポルフィリンは、光活性化光のエネルギーをトラップし、次いでそれを酸素分子に渡し、これを次に近隣の分子または構造を酸化することのできる励起状態にすることにより、触媒として働く。細胞死は、主としてDNAの損傷により引き起こされるのではなく、本質的膜構造の損傷により引き起こされる。

光化学療法は、現在、或るタイプの癌および乾癬を含む非悪性病変の治療に使われている。そのような療法の目標は、時には治癒（主に基底細胞癌について）であるが、通常は、

ばヘマトポルフィリンIX (HPIX)、ヘマトポルフィリン誘導体 (HpD) または「ジヘマトポルフィリンエーテル」(フォトフリンII) の静注後に強力なポルフィリン蛍光を示す組織の領域を同定するのに実験的に使用されている。そのようなポルフィリンは、半優勢的に悪性組織中に蓄積する傾向があるが、それらは損傷後に再生している組織または胚もしくは胎児の迅速に成長している組織にも蓄積する。正常な肝臓、脾臓および腎臓もまた、それらのポルフィリンを蓄積する傾向がある。そのような化合物および蛍光検出スコープを使用して、標準形式の外観検査により同定するには小さすぎる悪性組織の領域が気管支および膀胱において同定されている。

不運にも、HPIX、HpDまたはフォトフリンIIの静注後に少なくとも2週間（場合によっては2ヶ月以上）、臨床的に有意な（光感作）量のポルフィリンが皮膚中に存続する。このことは、患者が注射後の長期間の間、日光（直射または窓ガラスを通った日光）への暴露を避けなければならないことを意味する。理解できることだが、患者の応諾 (compliance) がしばしば乏しくなり、そしてポルフィリンの診断または治療的注射後の数週間は偶発的光毒症の「日焼け」が一般に起こる。持続性の光感作がこの方法に関係する主要な危険であり、そしてあまり広範に利用されない理由である。

癌の標準または常用の治療形式は、手術、放射線療法および化学療法である。しかしながら、光化学療法または光力学療法 (PDT) を含む他の治療形式も知られている。PDTは、経験に基づいて、幾つかの異なるタイプの癌並びに乾癬のよ

標準的な療法形式がおそらく有意な程度の効果を患者に与えるであろうと思われる時には、目標は局所コントロールによる緩和である。

メトキシソラレン (PUVA) 療法は、主に乾癬の治療に使われるが、皮膚に影響を及ぼすごく表面の癌（主にキノコ状真菌症）を治療するのに時々使われる。しかし、そのような治療には2つの深刻な問題点がある。第一は、この方法がヒトにおいて発癌性であると証明されていることである。第二は、光活性化光は大部分の組織に非常に強く吸収されるので、悪性組織を殺すことができる深さは、照射表面下の数ミリメートルに限定されることである。それらの問題点は、光化学療法に対するメトキシソラレンの有用性を厳しく制限する。

現在、光化学療法に最も一般的に使われているポルフィリンは、ヘマトポルフィリンIX (HPIX)、ヘマトポルフィリン誘導体 (HpD)、およびHpDの半精製形であるフォトフリンII (Photofrin II) である。ポルフィリンを光感作剤として使用する時、DNAの損傷よりもむしろ本質的膜構造の損傷により細胞死が生じる。従って、悪性の形質転換は深刻な問題とはならない。更に、ポルフィリンを光活性化するのに使われる可視（赤色）光は、メトキシソラレンを光活性化するのに使われる紫外光よりもずっと深く組織に貫通するので、ポルフィリン処理組織を殺すことができる深さがかなり大きい。また、或るタイプのポルフィリンは悪性組織に優勢的に蓄積する有意な傾向を示すので、近隣の正常組織に臨床上有意な損傷を引き起こすことなく悪性組織を破壊することが時々可

能である。

HplX、HpDおよびフォトフリンIIの全身適用の主な問題点は、それらの投与後数週間から数ヶ月の間、光感作濃度が皮膚に存続することである。結果として、皮膚中の光感作剤の濃度が無害なレベルに減少するまで患者が日光（直射または窓ガラスを通過したもの）を避けない限り、深刻な偶発的光毒皮膚反応が起こり得る。現在、ポルフィリンの投与後の光感作の問題は、注射後少なくとも2週間の間日光への（またはごく明るい人工光への）いかなる形態の暴露も回避し、そしてその後は非常に慎重に日光への暴露を開始するようにアドバイスすることにより、取り扱われている。これを実行するのは全く不便であるため、全ての患者がそれらの教示に従うわけではない。加えて、高い遮光力を有する日焼け止めの使用は、単に幾らか危険性を減らすだけであり、完全にそれを取り除くわけではないという警告と共に推められる。少ないケースでは、処理後1ヶ月以上もの間光感作が存在した患者に、偶発的な光毒障害を防ぐ試みとして数ヶ月間に渡り高い一日量でβ-カロチンが投与された。最後に、限定された領域に局所的に光感作剤を適用することにより、光毒性を減らす試みが行われている。

しかしながら、HplXまたはHpDをDMSO（ジメチルスルホキシド）Azone、または組織への拡散を増加させる目的の幾つかの他の賦形剤中において局所適用すると、別の種類の問題に出くわす。ポルフィリンがもはや組織に拡散できない（または溶液中に残存する）ような程度までDMSO Azoneが正常組

リンIXの合成を誘導するように、ヘムの生合成経路中のプロトポルフィリンIXの前駆体の有効量を前記患者に投与し、そして前記PpIXの光活性化作用スペクトル内の波長を有する光に前記病変を暴露し、それによって前記病変中に蛍光を誘導することを含んで成る方法を提供することである。

本発明の好ましい態様において、好ましいプロトポルフィリンIXの前駆体は、5-アミノレブリン酸として知られる5-アミノ-4-オキソペンタン酸であり、そして光活性化光の好ましい波長は、350-635nmの領域、より好ましくは約635nmの赤色光である。

好ましい態様の詳細な記載

天然に存在する光感作剤であるプロトポルフィリンIX (PpIX) は、ヘム生合成経路におけるヘムの直前駆体である。ヘムは種々の重要なヘム含有酵素の合成に必要であるので、全ての有核細胞は少なくともPpIXを合成する最小限の能力を有する。或るタイプの細胞および組織は、比較的少量のPpIXを合成することができる。正常条件下では、そのような組織におけるPpIXの合成は、細胞がヘムの要求にかなうのにちょうど十分である速度でPpIXを生産するような厳格なフィードバック制御下にある。しかしながら、この過程の通常の律速段階である5-アミノレブリン酸(ALA)の合成は、外因性ALA、ポルホピリノーゲンまたは他のPpIX前駆体の供給により迂回することができる。或る種の組織および器官は、それらが蛍光性で且つ光感作性になるほど大過剰のPpIXを蓄積

組織により希釈されるようになった時、ポルフィリンはたまたま存在する所で固定化されるようになる傾向がある。結果として、ポルフィリンの局所適用は悪性組織に対する特異性の低下と関係があり、そして適用部位の近くの正常組織がポルフィリンの局所的濃縮から持続性光感作を発生し得る。

発明の目的

本発明の目的は、誘導的発光による或るタイプの悪性および非悪性組織の検出方法を提供することである。

本発明の別の目的は、それ自体は光感作剤でないが生体内でプロトポルフィリンIX (PpIX)の合成を誘導する薬剤を使って全身的または局所的のいずれでも投与することができる光力学（光感作）治療方法を提供することである。

発明の記載

本発明の一つの観点によれば、患者の悪性および非悪性病変の検出方法であって、前記病変においてプロトポルフィリンIXの蓄積を誘導するように、ヘムの生合成経路中のプロトポルフィリンIXの前駆体の有効量を前記患者に投与し、そして前記プロトポルフィリンIXの吸光スペクトル内の波長を有する光に前記病変を暴露し、それによって前記病変において蛍光を誘導することを含んで成る方法を提供することである。

本発明の別の観点によれば、患者の皮膚、粘膜、子宮内膜および尿路細胞層(urothelium)の悪性および非悪性増殖過剰病変の処置方法であって、前記病変においてプロトポルフィ

するだろう。少なくとも皮膚の場合、PpIXはその場で合成されるように見える。Sigma Chemical Companyから市販されておりそして水溶性であるALAは、経口、局所または注射により投与することができる。経口または非経口経路は、体の至る所の或る種の良性および悪性組織中への臨床上有用な濃度のPpIXの誘導をもたらす。或るタイプの組織のみが、過剰のALAを供給した時に臨床上有用な量のPpIXを合成できるので、影響を受けた組織が光活性化光が到達できる部位にある場合にのみ、ALAの供給が有利である。現時点では、皮膚、粘膜（呼吸器、消化器および陰の）、子宮内膜および尿路細胞層(urothelium)の基底細胞癌、基底有棘細胞癌および有棘細胞癌並びに他の病変の処置が期待される。部位としては、(i) 皮膚および結膜；(ii) 口、咽頭、食道、胃、腸および腸付属器、直腸並びに肛門管の内層；(iii) 鼻道、鼻腔、鼻咽頭、気管、気管支および細気管支の内層；(iv) 尿管、膀胱および尿道の内層；(v) 膣、子宮頸および子宮の内層；(vi) 壁側胸膜および肺胸膜；(vii) 腹腔および骨盤腔の内層、並びにそれらの腔の内部に含まれる器官の表面；(viii) 硬膜および髄膜；(ix) 直接的に、手術時に、または針を通して挿入した光ファイバーにより、光活性化光に対してアクセシビリティにされ得る固体組織中の任意の腫瘍、に関わる病変が挙げられる。

入射赤色光(600-700nm)の1~10%が厚さ1cmのヒト組織スラブを通過できる一方、青色光(約400nm)はわずか0.001%かそこらが同じ厚さのヒト組織を通過できることが

示されているので、光活性化光の波長は幾らか重要である。従って、光感作剤が強力に赤色光を吸収するならば、より好結果となるであろう。PpIXは赤色光を強力に吸収する。本アプローチは、従来技術を上回る幾つかの利点を有する。第一に、PpIXは、正常組織においてHpIX・HpDまたはフォトフリンIIよりもずっと短い半減期を有する。これは処置後における偶発的光毒性皮膚反応の危険を大きく減らす。第二に、或るタイプの病変へのALAの局所適用は、それらの病変内部でPpIXを誘導することができるが、その他の場所では誘導しない。このことは、処置の特異性を改善し、偶発的な光毒性反応をごく低レベルに減らし、そして均一有効量のALAを全身的に投与しようとしたならば全身が暴露されたであろうALAとPpIXの両方の量を大きく減少させる。ALAとPpIXは両方とも普通の代謝産物であり、そして体内の生化学的機構により非常に容易に処理される。しかしながら、非常に多量のALAは（多量のHpIXまたはHpDと同様に）、運動神経伝達速度の一時的減少と関係があるので、ALAの用量をまだ有効である最小量に減らすことが望ましい。局所適用は、全身投与よりもずっと少ないALAを要求する。第三に、PpIXは光活性化光により迅速に不活性化される。治療線量の光活性化光へのPpIX含有組織の暴露後、処置容量内部の組織の光感作の実質的減少がある。その結果、特定の病変へのALAの局所適用によりPpIXが誘導されれば、深刻な光毒症の危険なしに処置後すぐに患者を太陽に暴露することができる。第四に、経口、局所または注射により投与すると、ALA

ALAはPpIXの効果的な誘導物質である。対照的に、HpIX・HpDおよびフォトフリンIIは、ほとんどの場合、注射により投与した時のみ効果的である。このALAの多能性は、医者達による日常使用への近づきやすさを増大させる。というのは、経口および局所の投与経路は、非経口よりもずっと便利だからである。第五に、ALAの投与により光感作され得る正常および異常組織は、HpIX・HpDまたはフォトフリンIIの投与により光感作され得るものと幾らか異なる。従って、ALAは、他の光感作剤が有用でない臨床状況において有用となり得る。

本発明の技術は、既に実施できるものを実施する別の方法であるだけでなく、実際、治療能力の有意な進歩である。

実施例 1

右頬と下顎骨の再発性上皮内癌細胞癌を有すると診断された87才の患者を、病変あたり 100mgのALAの投与量で17% (w/w) Glaxal基剤中のALAの局所適用により処置した。適用の2.5時間後、病変を光活性化光、即ち赤外（熱フィルター）および 600nm以下の波長（Hoya R-60フィルター）を除去するために遮断された 500ワットのタンダステンランプの出力の光に、52.5mW時/cdの線量（強度×時間）において暴露した。処置後40日間患者を評価し、病変が完全に応答を示したと判断された。

実施例 2

右耳の上部後方および外側に、上皮内癌細胞癌を有すると診断された73才の患者を、病変あたり35mgの投与量におい

て10% (w/w) Glaxal基剤中のALAの局所適用により処置した。ALAの適用の3時間後、病変を実施例1に記載の光源からの26mW時/cdの光活性化光に暴露した。処置後21日間の評価は、完全な応答を示した。

実施例 3

次の部位に多発性有棘細胞癌を有すると診断された64才の患者：

- (1) 背、左肩
- (2) 背、右胸郭
- (3) 背、右胸郭下方
- (4) 左手背側面、指の近く
- (5) 左手背側面、中央部
- (6) 左手、母指関節付近（約10mm隆起）

の病変1、2および3を、20% w/w Glaxal基剤中病変あたり20mgのALAで処置した。3時間後、50mW時/cdの線量において実施例1に記載の光源からの光活性化光に暴露した。処置の10日後、病変1はほとんど完全な応答を有し、病変2は部分的な応答、そして病変3は完全な応答を有した。次いで、病変1および2並びに病変4、5および6を10% w/w Glaxal基剤中の22mgのALAで3時間処置し、そして下記の線量：

- | | |
|------|----------|
| 病変 1 | 17mW時/cd |
| 病変 2 | 17mW時/cd |
| 病変 4 | 26mW時/cd |
| 病変 5 | 26mW時/cd |

病変 6 ————— 26mW時/cd

において、上述の光活性化光に暴露した。処置後25日間、患者は次のように評価された：

- | | |
|------|------------------|
| 病変 1 | 完全な応答 |
| 病変 2 | 完全な応答 |
| 病変 4 | 再発なし |
| 病変 5 | 部分的応答 |
| 病変 6 | 10mmの隆起の約3mmの低下。 |

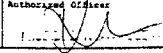
実施例 4

43才の患者は、(1) 背、左肩および(2) 背、高腰椎領域、右側の基底細胞癌を有すると診断され、この患者を33% w/w Glaxal基剤中病変あたり50mgのALAで3時間処置した。次いで実施例1に記載の光源から37mW時/cdにおいて病変を光活性化した。処置後64日間の評価は両病変の完全な応答を示した。

実施例 5

ALAを等張塩溶液に溶かし、次いで皮下または腹腔内注射のいずれかにより、体重1kgあたり 100~500 mgの用量においてマウスに全身投与した。3時間後、マウスを犠牲にし、子宮の凍結切片を取った。それらの切片を蛍光顕微鏡により調べると、子宮内膜は強いプロトポルフィリン蛍光を示したが、下層の子宮筋層は示さなかった。ALAを全身的に投与したので、それは確実に子宮筋層中に存在していたにちががなく、そして子宮筋層におけるプロトポルフィリン蛍光のその後の欠失は、過剰の外因性ALAを供給した時のことを示

すにちがいない。従って、ALAを子宮内膜の表面に直接適用する場合、子宮筋層は光感作性にならないであろうし、そして光活性化光への子宮内膜と子宮筋層のその後の暴露は子宮内膜組織の優先的切除をもたらすであろう。

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DECLARATION		
<p>This International Searching Authority hereby declares that no international search report will be established on the above-identified international application for the reasons indicated below. (1)</p> <p>1. The subject matter of the international application relates to: (2)</p> <p>a. ☐ scientific theories.</p> <p>b. ☐ mathematical theories.</p> <p>c. ☐ plant varieties.</p> <p>d. ☐ animal varieties.</p> <p>e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes.</p> <p>f. ☐ schemes, rules or methods of doing business.</p> <p>g. ☐ schemes, rules or methods of performing purely mental acts.</p> <p>h. ☐ schemes, rules or methods of playing games.</p> <p>i. ☒ methods for treatment of the human body by surgery or therapy.</p> <p>j. ☐ methods for treatment of the animal body by surgery or therapy.</p> <p>k. ☐ diagnostic methods.</p> <p>l. ☐ mere presentations of information.</p> <p>m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art.</p> <p>2. The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out: (3)</p> <p>a. ☐ the description.</p> <p>b. ☒ the claims.</p> <p>c. ☐ the drawings.</p> <p>Comment: International Classification:- A 61 K 31/195</p>		
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5-Aminolävulinsäure-Nanoemulsion

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The present invention relates to a composition comprising a nano-emulsion that contains 5-aminolevulinic acid as well as a carrier in an aqueous phase. This invention also relates to a pharmaceutical preparation containing this composition. The nano-emulsions of this type can be used in photodynamic therapy as well as in the photodiagnostic detection of proliferative cells.

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(54)【発明の名称】 5-アミノレブリン酸-ナノエマルジョン

(57)【要約】

本発明は、5-アミノレブリン酸及び担持剤を水相中に含むナノエマルジョンを含む組成物及びこの組成物を含有する薬剤学的製剤に関する。このようなナノエマルジョンは、増殖性細胞の光力学的治療の際に及び光診断学的検査のために使用される。

【特許請求の範囲】

【請求項1】 ナノエマルジョン、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された作用物質及び担持剤を水相中に含有することを特徴とする組成物。

【請求項2】 乳化された粒子の平均寸法は $\leq 10 \sim 200$ nmである、請求項1に記載の組成物。

【請求項3】 担持剤は脂質1種以上から及び乳化剤1種以上から形成されている、請求項1又は2に記載の組成物。

【請求項4】 乳化剤は、グリセロ磷脂質1種以上を、脂質：乳化剤の質量比 $0.05 \sim 0.4 : 1$ で含む、請求項2に記載の組成物。

【請求項5】 作用物質は、組成物の全質量に対して $1 \sim 25$ 質量%、殊に $5 \sim 15$ 質量%の配分で存在する、請求項1から4までのいずれか1項に記載の組成物。

【請求項6】 更に、化粧品学又は製薬学で慣用である助剤及び／又は添加剤を含有する、請求項1から5までのいずれか1項に記載の組成物。

【請求項7】 ゲルの形で存在し、組成物の全質量に対して作用物質 $5 \sim 15$ %、担持剤 $45 \sim 55$ %、助剤 $1 \sim 5$ %及び残りは水を含む、請求項6に記載の組成物。

【請求項8】 ローシヨンの形で存在し、組成物の全質量に対して作用物質 $5 \sim 15$ %、担持剤 $15 \sim 25$ %、助剤 $15 \sim 25$ %及び残りは水を含む、請求項6に記載の組成物。

【請求項9】 室温で1年貯蔵の後の作用物質の含分が 5 %より多くは減少していない、請求項1から8までのいずれかに記載の組成物。

【請求項10】 薬剤学的製剤の形である、請求項1から9までのいずれか1項に記載の組成物。

【請求項11】 局所適用可能である、請求項10に記載の組成物。

【請求項12】 請求項1から11までのいずれか1項に記載の組成物を製造する方法において、担持剤及び水相を含む混合物を製造し、ナノエマルジョンに変換し、その際、ナノエマルジョンに変換する前及び／又は後に作用物質を添

加し、その後、場合により助剤及び／又は添加剤を加えて混合することを特徴とする、請求項1から11までのいずれか1項に記載の組成物の製法。

【請求項13】 酸素遮断下及び／又は光遮断下に操作する、請求項12に記載の方法。

【請求項14】 5～45℃の温度で操作する、請求項12又は13に記載の方法。

【請求項15】 光学的治療における、5-アミノレブリン酸、その誘導体、前駆物質又は代謝産物から選択された作用物質を含有するナノエマルジョンの使用。

【請求項16】 ナノエマルジョンを局所的に適用する、請求項15に記載の使用。

【請求項17】 細胞増殖に結びついている疾病の治療における、請求項15又は16に記載の使用。

【請求項18】 腫瘍疾病の治療における、請求項17に記載の使用。

【請求項19】 疾病は、基底細胞癌、扁平上皮癌、ボウエン病、化学線角化症、尖圭コンジローム（CIN）、陰門の内皮腫瘍形成（VIN）又は瘤状又は皮下の癌疾病である、請求項18に記載の使用。

【請求項20】 疾病は乾癬である、請求項17に記載の使用。

【請求項21】 光学的治療用医薬品の製造のための、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された作用物質を含有するナノエマルジョンの使用。

【請求項22】 光学的治療法において、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された作用物質を含有するナノエマルジョンを羅病生体組織に有効量で適用し、処置すべき組織中に作用物質の十分な量を配量するために好適である時間インキュベートし、かつこの組織に光を照射することを特徴とする、光学的治療法。

【請求項23】 増殖性細胞の検出のための、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された作用物質を含有するナノエマルジョンの使用。

【請求項24】 腫瘍疾病の診断のための、請求項23に記載の使用。

【請求項25】 請求項11に記載の局所適用可能な組成物及び

次のものから選択された少なくとも1つの構成成分：

- (a) 実質的に光不透過性の枚葉状材料
- (b) この枚葉状材料を適用位置上に固定するための手段及び
- (c) 組成物を適用位置上に施与するための手段

を含むキット。

【発明の詳細な説明】**【0001】**

本発明は、5-アミノレブリン酸、その誘導体、前駆物質又は代謝産物を含むナノエマルジョンに関する。

【0002】

光力学的治療は、細胞増殖と関連している種々の前悪性及び悪性の疾病を処置するための新規のかつ期待される方法である。この光力学的治療の原理は、いわゆる光増感剤を腫瘍組織中に入れ、これを適当な波長の光の照射によって細胞毒活性物質に変換し、これが最終的に細胞を破壊する作用をすることに基づく。この方法の選択性は、正常組織に比べて急速に増殖する腫瘍細胞中のこの増感剤の著しい富化に基づく。局所的に限られた光照射により、この腫瘍組織中に含有された増感剤が目的に合って活性化され、これにより、健康な組織の十分な保存下に癌細胞が破壊される。

【0003】

従来は、光増感剤として、大抵はヘマトポルフィリン誘導体の静脈適用可能な混合物が使用されていた。種々の癌で勇気付けられるような臨床結果が得られているにも関わらず、このヘマトポルフィリン誘導体は種々の欠点を有する。第一に、低い腫瘍選択性および身体からの緩徐すぎる放出の故に、正常組織中に比較的高い作用物質濃度が現れる。その結果、照射の際に、健康な組織中で不所望の光化学反応が起こる。第二に、この処置は一般的な光感受性を生じるので、患者に約4週間の間日光を当ててはならない。

【0004】

正常組織中の高い作用物質濃度及びそれに伴う不所望な副作用の減少は、特定の場合、殊に皮膚科学的及び婦人科的使用の場合には、公知の全身的処方物の代わりに局所的に適用可能な作用物質処方物の開発により達成することができる。光感受性を減少するために、更に、光化学的に不活性で、目標細胞内で初めて光増感剤に変換される、光増感剤の前駆物質を使用する試みがなされている。

【0005】

5-アミノレブリン酸は、グリシン及びスクシニル-CoAから合成される生

体特有の物質である。ヘムー生合成の領域では、5-アミノレブリン酸（5-ALA）から、迅速に進行する多くの反応工程で、高度な光活性プロトポルフィリンIXが生じ、これは引き続き、緩徐な反応で、ヘムに変換される。天然の調節メカニズムは、高すぎるヘム濃度の場合に、5-アミノレブリン酸の生体特有の合成をもプロトポルフィリンIXの分解をも抑制する。

【0006】

合成された5-アミノレブリン酸の外からの適用によりこの調節メカニズムは避けられ、これがプロトポルフィリンIXの高い生産をもたらす。天然のコントロールメカニズムによるその分解が更に抑制されるので、このプロトポルフィリンIXが細胞中に増加する。プロトポルフィリンIXは、光の照射の際に光化学的酸化反応を開始することができ、それに伴い光増感剤として作用することができる。この増感剤分子による光量子の吸収の際に、これは、先ず1電子の励起された状態（シングレット状態）に変えられ、この状態は比較的短命であり、その過剰エネルギーを数ナノ秒以内に蛍光光子の放射により再び放出するか又は比較的長命のトリプレット状態に移行する。このトリプレット状態から、エネルギーは細胞中に存在する酸素分子上に移されうる。

【0007】

この際に生じるシングレット-酸素は、細胞成分、例えば細胞膜及びミトコンドリアと反応するか又は細胞障害性ラジカルの形成を引き起こすので、殊に増殖性細胞上に細胞毒性作用をする。更に、この光増感剤の照射は、特徴的な蛍光線をもたらし、これを、検出反応のために、例えば増殖性細胞の検出のために使用することができる。

【0008】

技術水準からは、局所的に適用可能な5-アミノレブリン酸-組成物の使用下での一連の研究が公知である。この研究に共通していることは、使用される5-アミノレブリン酸が水中油型-エマルジョンの形で存在することであるが、違いは、他のパラメータ、例えば浸透時間、処置期間、使用光の種類及び当てられる光用量である。

【0009】

B. Thiel 等 (H+G, Band 69, Heft 3, 161-164頁(1994) は、水中油型－エマルジヨンの形の20% δ －アミノレブリン酸の使用下での、5～6時間の浸透時間及びアルゴンイオンポンプカラーレーザー（放射最大630nm）を用いる50～100 J / cm^2 の積分全用量での引き続く照射による研究を記載している。

【0010】

Wolf 等(Journal of the American Academy of Dermatology Vol. 28, 17-21頁, 1993) は、水中油型－エマルジヨンの形の20% γ －アミノレブリン酸の使用下での、4、6又は8時間の浸透時間及び非フィルター光又は赤色光を用いる30 J / cm^2 ～100 J / cm^2 の光用量での照射による研究を記載している。

【0011】

技術水準から公知のこれらの研究は γ －アミノレブリン酸の使用下での光力学的治療の期待できる可能性を明らかに示しているが、従来公知の水中油型－エマルジヨンには一連の欠点が付随している。

【0012】

例えば、M. Novo Rodriguez 等(SPIE, Vol. 2371, 204-209頁) は、アミノレブリン酸が臨床使用のために必要な高い濃度で、中性～塩基性のpH領域で水溶液中で不安定であることを示している。5.01のpH値の場合にのみ、25時間の研究時間で満足しうる結果が得られ、 γ －アミノレブリン酸水溶液にとっての最適条件としては、3%の濃度及び5のpH値が挙げられている。しかしながら、臨床的使用のためには一般に、高い濃度範囲の組成物を供給することも、更に市場での使用のためには、週間又は月の大きさの5-ALA溶液の安定性も必要である。

【0013】

V. von Arex 等.(J. Pharm. Pharmacol. 49 : 652-656, 1997) は、種々のゲル中での γ －アミノレブリン酸の局所的適用のための研究を記載している。 γ －アミノレブリン酸の安定性を保持するための最良の処方として、pH<6でのNovion AA-1、ポリアクリル酸との組み合わせが記載されている。

【0014】

公知の水中油型エマルジョンのもう一つの欠点は、障害組織中への光増感剤の浸入深さが最適ではないことにある。これにより、多くの場合に、羅病組織は、光増感剤の活性化のために使用された光の浸入深さがより深い所の層の処置も可能であるにも関わらず、その表面層中のみでこの光力学的治療が使えるだけである。

【0015】

従って、本発明の課題は、技術水準から公知の欠点が少なくとも部分的に除かれていて、殊に充分な安定性を有し、かつ組織中への改善された浸入深さを示す、5-アミノレブリン酸含有組成物を提供することであった。

【0016】

この課題は、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された物質を含むナノエマルジョン及び担持剤を水相中に含有することを特徴とする組成物により解決される。

【0017】

意外にも、5-アミノレブリン酸の安定性は、ナノエマルジョン中への処方の際に著しく高めることができることが確認された。この原因は知られていないが、ナノソームから生じるマイクロ環境が5-アミノレブリン酸の安定性に特に好適に作用すると思われる。

【0018】

更に意外にも、本発明によるナノエマルジョンを用いて非常に高い組織侵入深さを得ることができ、これにより深部に存在する疾病又は高い層厚の疾病も処置に使えることが明らかになった。従来は5-アミノレブリン酸がその小さい寸法の故に直ちに容易に、例えば炎症、癌前駆症及び腫瘍の上に存在する損傷された表皮を通して浸入できることから出発していたので、この大きい浸入深さは殊に意想外のことであった。

【0019】

第三の意想外の利点は、本発明によりナノエマルジョン中に包埋された5-アミノレブリン酸は、明らかに非常に良好に細胞により吸収されることである。こ

れにより、一方で、改善された目標合わせが達成され、他方で、浸入時間、即ち組成物の施与と疾病組織の光照射との間の時間が短縮され、これは患者にとっては好ましい軽減である。

【0020】

本発明によれば、ナノエマルジョンは、5-アミノレブリン酸、その誘導体、前駆物質及び／又は代謝産物から選択された作用物質を含有する。「誘導体」とは、殊に塩、錯体及び付加化合物と理解すべきである。ここで、「前駆物質」及び「代謝産物」とは、細胞内でプロトポルフィリンIXに変換されるような物質と理解すべきである。作用物質は5-アミノレブリン酸又はその誘導体が特に有利である。担持剤は、それが水相中でナノエマルジョンを形成することのできるかぎりにおいて、任意の担持剤であってよい。有利に、担持剤は、油相、即ち水と混じらない物質、例えば脂質並びに乳化剤を含む。生理学的に無害な担持剤物質を使用するのが有利である。

【0021】

ナノエマルジョン中に乳化される粒子（ナノソーム）の大きさは、平均して $\leq 200\text{ nm}$ 、例えば $10\sim 200\text{ nm}$ である。それぞれ最適な粒径は、他のパラメータ、例えば組成物の粘度に依存する。例えば 5 mPas の粘度を有するゲルを用いると、約 110 nm の平均粒径で良好な結果が得られ、同様に 1.6 mPas の粘度のローションには、約 20 nm の平均粒径で良好な結果が得られた。

【0022】

長時間にわたり安定であり、界面活性剤及び界面活性助剤の高い濃度を有せず有毒な乳化剤複合体を含有しない好適な担持剤系は、例えばUS-特許第5152923号明細書に開示されている。このナノエマルジョンは、乳化剤としてグリセロ燐脂質、例えばレシチン又はケファリンを、かつ油相として生理学的に認容性の脂質、たとえばトリグリセリド、例えば植物又は動物油、例えば落花生油、大豆油などを含む。乳化剤／油の質量比は $0.05\sim 0.4:1$ である。

【0023】

実際に既に5-アミノレブリン酸-ナノエマルジョン中で有効に使用されている乳化剤は、例えば卵レシチン、大豆レシチン及びホスファチジルコリンである

。定評のある脂質は、例えばミグリオール812である。

【0024】

組成物中の作用物質、例えば5-アミノレブリン酸の配分は、主として所定の用途に依存して決まる。一般に、組成物の全質量に対して約1～25質量%が存在する。しかしながらより高い又はより低い配量も可能である。光力学的治療と関連している用途のためには、5～15質量%、殊に約10質量%の配分が好適であると立証されている。

【0025】

この組成物は、更に助剤及び／又は添加剤、殊に化粧品学又は製薬学で慣用であるような物質を含有することができる。このような物質の例は、例えば緩衝剤、安定剤、付加的乳化剤、濃化剤等である。

【0026】

特に有利な1実施形では、本発明による組成物は、組成物の全質量に対して作用物質1～25質量%、有利に5～15質量%、担持剤40～60質量%、有利に45～55質量%、助剤0～10質量%、有利に1～5質量%及び残りは水を含有するゲルである。

【0027】

もう一つの有利な実施形によれば、本発明の組成物は、組成物の全質量に対して作用物質1～25質量%、有利に5～15質量%、担持剤10～30質量%、有利に15～25質量%、助剤10～30質量%、有利に15～25質量%及び残りは水を含有するローションである。

【0028】

先に記載のように、本発明による5-アミノレブリン酸一組成物は、意想外に高い貯蔵安定性を示し、この際、1.5～3のpH値を有する組成物中の作用物質分は、室温で1年貯蔵の後にも、有利に5%以上、特に有利に4%以上は減少していない。5℃で1年貯蔵の後には、作用物質分は有利に3%以上、特に有利に2.5%以上は減少していない。

【0029】

本発明のもう一つの課題は、薬剤学的製剤の形の本発明の組成物である。この

場合には、組成物は薬剤学的に受け入れられない成分を含有せず、特に例えば刺激を起こす成分を含有しない。この薬剤学的製剤は、既に記載の担持剤物質と並んで、受け入れ可能な、かつ特に良好な認容性である更なる助剤及び／又は添加剤を含有することができる。

【0030】

薬剤学的製剤は、全身的適用に好適である形で、例えば注射可能な液体の形で存在することができる。しかしながら、この製剤は、皮膚科及び婦人科の用途のためには局所適用に好適である形で存在するのが有利である。この製剤は、それぞれの所望の適用形に好適な特性、例えば、適用の後に5-アミノレブリン酸で処置されたナノソームが目標細胞中へ十分に浸入することを確保するために粘度及び流動性を有する。これらの粘度及び流動特性は、濃化剤、例えばポリエチレングリコールステアリルエーテル、ポリエチレングリコールステアレート及び／又は多糖類、例えばポリサッカライドB-1459の添加により調節することができる。

【0031】

本発明のもう一つの課題は、本発明の組成物又はその薬剤学的製剤の製法である。この際、担持剤物質の成分を水相中に予め装入し、この混合物を強い均質化によりナノエマルジョンに移行させる。このために、例えば市場で入手可能な高圧ホモジナイザーを使用することができる。5-アミノレブリン酸及び場合によって存在する添加剤を均質化の前及び／又は後に添加することができる。ナノエマルジョンの製造後に、更なる助剤及び添加剤（均質化の際にはそれらの存在は不所望であった）を加えることができる。

【0032】

この方法を空気遮断下に、例えば真空にすること及び／又は保護ガス雰囲気を用いて実施するのが有利である。更に、光遮断下に操作するのが有利である。この方法は、所望のナノエマルジョンの形成を起こすことができ、成分、殊に作用物質の十分な安定性が与えられる温度で実施する。一般に、約5～45℃の温度範囲が好適であると立証された。しかしながら、例えば先ず別のバッチ中で混合され、かつ場合によっては均質化され、その後に初めてこの組成物に添加される

助剤及び／又は添加剤の加工は、例えば約80℃までの高い温度で行うことができる。薬剤学的用途のためには、例えば無菌出発物質の使用により、かつ無菌の方法条件の保持により及び／又は製造後の滅菌工程により、生じる生成物の滅菌に配慮すべきである。

【0033】

本発明による組成物の主要な使用分野は光力学的治療の分野にあり、この際、ナノエマルジョンが特に有利に局所的に適用される。本発明によるナノエマルジョンの使用は、その克服が、5-アミノレブリン酸から形成される増感剤の光活性化を用いる細胞又は組織の増殖抑圧又は死滅化を包含する全ての疾病で可能である。これには、殊に増加性細胞増殖と結びついている疾病が挙げられる。それというのも、この場合には、疾病細胞中の増加した細胞代謝により光増感剤の特に高い富化が起こるからである。

【0034】

従って、本発明による組成物は、腫瘍疾病、例えば基底細胞癌、扁平上皮癌、ボウエン病、化学線角化症、尖圭コンジローム（CIN）、陰門の内皮腫瘍形成（VIN）又は瘤状又は皮下の癌疾病の処置のために好適である。非腫瘍性疾病の例は乾癬である。

【0035】

処置は、例えば、作用物質、例えば5-アミノレブリン酸を含有するナノエマルジョンの局所的適用及び引き続く処置すべき組織中への5-アミノレブリン酸の充分量の浸入を行なわせるためのインキュベーションにより行う。このインキュベーションの間には、処理された位置の上への光照射は、不所望の早すぎる活性化を避けるために、例えばカバーにより避けるのが有利である。一般に約1～8時間、通常は約4時間であるインキュベーション時間の経過の後に、この組織に光源を用いて充分量の線量を照射する。好適な光源には、白色光を放射するランプ並びに単色光源、例えばレーザー、殊に約630nmで放射するアルゴン-カラーレーザーが包含される。線用量は、通常は、1回使用当たり約20J/cm²～数100J/cm²の範囲内にある。

【0036】

本発明によるエマルジョンのもう一つの使用分野は、試料、例えば組織試料中の増殖性細胞の存在の検査に関する。この検査は、正常細胞と比べて増殖性細胞中の作用物質の代謝により得られる光増感剤の選択的増加に基づく。作用物質は、5-アミノレブリン酸及び光増感剤はプロトポルフィリンIXが有利である。光増感剤の富化は、光診断法により、例えば405nmの波長の光を照射し、この光増感剤により得られる蛍光線の測量により測定することができる。本発明によるナノエマルジョンは、殊に腫瘍診断学での使用に好適である。

【0037】

本発明のもう一つの課題は、本発明によるナノエマルジョンを光力学的治療用の医薬品の製造のために使用することである。

【0038】

最後に、本発明は、本発明により局所的に適用するのに好適であるナノエマルジョン並びに1以上の補助材を含有するキットに関する。このような補助材は、例えば処置すべき位置の上にナノエマルジョンを施与した後に施こされる、光による早すぎる活性化を阻止するためのプラスチックシートのようなカバー材料、このカバー材料の固定用の手段又はナノエマルジョンを処置すべき位置の上に施与するための手段である。

【0039】

次の実施例につき本発明を更に詳説する。

【0040】

例

1. 10% 5-アミノレブリン酸-ローションの製造

US-特許第5152923号の方法により、燐酸塩緩衝液中の卵レシチン（ホスファチジルコリン83%）、ミグリオール812（トリグリセリド）及びポリソルバツム80からナノコロイド担持剤系を製造した。この担持剤系の分析データを次の第1表に記載した。

【0041】

【表1】

第1表

水相	磷酸塩緩衝液 20 mM, pH 6.0
光学的特性	黄色で強い玉虫色に輝く液体
室温での pH	6.0
粘度 (20℃)	1.6 mPas
ナノ粒子の寸法	≤ 10-200 nm
平均粒径	19.4 nm
卵レシチン含分	17.5 mg/ml
ポリソルバツム 80 含分	≤ 3% (w/w)
ミグリオール 812 含分	34-38 mg/ml
50 ml 中の好気性中温菌	< 1 CFU/ml

【0042】

5-A L A-ナノコロイドローションの製造のために使用された成分及びそれらの相対的配分を第2表中に記載した。

【0043】

【表2】

第2表

名 称	量 (質量%)
相 1	
セチルアルコール	5.00 %
ステアリルアルコール	1.00 %
グリセリンモノステアレート	2.00 %
ワセリン脂肪 SNOWWHITE	2.00 %
薬用流動パラフィン	2.00 %
化粧品用イソプロピルミリステート	4.00 %
クレモフォール A 25	1.00 %
クレモフォール S9	1.50 %
クレモフォール EL 00647	1.88 %
相 2	
水	48.87 %
ソルビトール 70 %	0.25 %
フェノキシエタノール	0.50
相 3	
ナノコロイド (第1表)	20.00 %
5-アミノレブリン酸-塩酸塩	10.00 %

【0044】

全ての方法工程を、光及び空気酸素の遮断下を実施した。第2表による成分を記載の量比で80℃で一緒に融解させ、かつ引き続き混合することにより相1を製造した。

【0045】

別の容器中で相2を準備した。このために、水を予め装入し、第2表による残りの成分を攪拌下に添加した。十分な混合の後に相2を80℃まで加温し、真空下に相1に添加混合した。

【0046】

75℃まで冷却の後に、この混合物をホモジナイザー中で2分間均質化した。

生じた混合物を60℃まで冷却し、改めて2分間均質化した。

【0047】

別の容器中で真空下および光遮断下に、相3を製造した。このために、前記のようなナノコロイド担持剤系を予め装入し、25～30℃で5-アミノレブリン酸塩酸塩をこの中に溶解させた。引き続き、相3を40℃で真空下に相1と相2との混合物に加えた。その後、この組成物に保護ガスを吹き込み、ホモジナイザー中で2～3分間均質化した。引き続き、攪拌下に室温まで冷却させた。

【0048】

作用物質の長時間安定性の測定のために、このローションの一部を貯蔵試験に供した。5-ALA-含分は、5℃で1年貯蔵の後に、当初含分の97.92%であり、室温では同じ時間で96.50%の値が得られた。

【0049】

2. 10%5-アミノレブリン酸ゲルの製造

US-特許第5152923号の製法により、K/Na 燐酸塩緩衝液中の卵レシチン及びミグリオール812（トリグリセリド）からナノコロイド担持剤系を製造した。分析データを次の第3表に記載した。

【0050】

【表3】

第3表

水相	磷酸塩緩衝液 20 mM, pH 6.0
光学特性	乳様液体
室温での pH	6.0
20 °C での粘度	1.5 mPas
ナノ粒子の寸法	≤ 10-200 nm
平均粒径	110.6 nm
標準偏差	32.1 %
全脂質－含分	105.4 mg/g
レシチン－含分	27.0 mg/g
ミグリオール 812－含分	78.4 mg/g
100 ml 中の好気性中温菌	< 1 CFU/ml

【0051】

5－アミノレブリン酸－ナノコロイドゲルの製造のために使用された成分及びそれらの相対的配分を第4表に記載した。

【0052】

【表4】

第4表

名 称	量 (質量%)
相 1	
水	38.30 %
ケルトロール	1.70 %
相 2	
ナノコロイド (第3表)	50.00 %
アミノレブリン酸－塩酸塩	10.00 %

【0053】

相1の製造のために、水を予め装入し、60～70℃まで加温し、引き続き真空下にケルトロールをその中に分散させた。工程1でこの混合物を4分間均質化

させ、その後、攪拌下に工程1で30℃まで冷却させた。

【0054】

相2の製造のために、このナノ担持剤系を閉鎖容器中に真空下、室温で予め装入し、5-アミノレブリン酸塩酸塩を攪拌下に2～3時間かけて完全に溶解させた。

【0055】

その後、相2を真空下に相1に混合し、引き続き窒素を吹き込んだ。生じた組成物を最大30℃の温度で攪拌下に2時間均一に混合した。

【0056】

作用物質の長時間安定性の測定のために、このゲルの一部を貯蔵試験に供した。5-ALA-含分は5℃で1年貯蔵の後に、当初含分の99.17%であり、室温では同じ時間で98.94%の値が得られた。

【0057】

3. 例1のナノコロイドローションの使用下での光力学的治療

本発明によるナノローションの作用効果を、臨床研究で19人の患者集団中の55基底細胞癌で研究した。

【0058】

ナノコロイドローションの施与の前に、処理すべき全皮膚面をアルコール溶液で清浄化した。それぞれ処理すべき皮膚面1cm²当たりナノコロイド溶液0.15gを施与したら、これは薄い可視ローション膜をもたらした。この施与の後に、ローションの汚れ及び室内光により惹起される不所望の光力学的反応を阻止するために、全面を光不透過性のカバー材料で覆った。6時間の作用時間の後に、カバーを除き、プロトポルフィリンIXの存在及び腫瘍の寸法を、紫外線での照射の際のポルフィリンの特徴的赤色蛍光を用いて評価した。

【0059】

この照射は、全可視領域にわたるスペクトル分布を有する250Wハロゲンランプからの非フィルター光を用いて約800nmの最大で実施した。全ての障害に、10cmの間隔で照射し、このことは10cmまでの直径を有する領域の照射を可能とした。照射時間は、200mW/cm²の強度で20分であり、24

0 J / cm²の全光用量に相当した。

【0060】

患者集団は、転移のない1以上の表面的基底細胞癌を有する19人を含む。合計55の基底細胞癌を光力学的治療により処置した。この研究で採用した患者のどれも予め慣用法又は光力学的治療の処置はなされていなかった。患者の年齢は32～93歳であり、平均年齢は65歳であった。14患者（73.7%）は男性であり、5患者（25.3%）は女性であった。1例外を有して、この研究で処置された皮膚腫瘍は表面的な障害であった。障害の平均直径は、13.2 mmであり、寸法変動は4.0～45 mmの間であった。種々の身体領域の処置腫瘍の数は、頭部及び頸部で11（20%）、胴体部で37（67%）、上部四肢で3（5%）及び下部四肢で4（7%）であった。この処置の開始前に、診断を確認するために通常のバイオプシーを得た。治療結果を目による検査及び触によりで、かつ腫瘍の26（47%）では組織病理学的検査によっても評価した。再検査の際の処置位置の臨床的に確認可能な腫瘍の不存在を腫瘍完全応答と定義した。腫瘍寸法の著しい減少を腫瘍部分応答と定義した。

【0061】

この研究で達成された応答率（Ansprechraten）を第5表中にまとめた。19患者で処置された55基底細胞癌の47（85%）は、1回の処置の後に、処置後少なくとも6ヶ月後の再検査によっても同様に臨床的に確認されるように完全に消失することが確認された。残りの8基底細胞癌（15%）では部分的消失、即ち腫瘍寸法の著しい減少が確認された。

【0062】

第6表は、基底細胞癌の限局部位に依存する光力学的治療の結果を示している。最良の結果は、四肢上の7障害で得られ、これらは完全に消失した。37胴体部障害のうち32腫瘍は完全に消失し、頭部及び頸部の11腫瘍の8（76%）は完全に消失した。

【0063】

【表5】

第5表

	目による評価	バイオプシー
患者の数	19	13
基底細胞癌	55	26
完全消失	47 (85%)	21 (81%)
部分消失	8 (15%)	5 (19%)
反応なし	-	-

【0064】

【表6】

第6表

	頭部及び頸部	胴体部	四肢
患者の数	6	12	4
基底細胞癌	11	37	7
完全消失	8 (73%)	32 (86%)	7 (100%)
部分消失	3 (27%)	5 (14%)	-
反応なし	-	-	-

【0065】

4. 例2によるナノコロイドゲルの使用下での光学的治療

ゲルの形の本発明によるナノエマルジョンの作用効果を、47障害の尖圭コンジローム及び陰門の内皮腫瘍形成(VIN)の光学的治療の臨床研究で、年齢18～45歳(平均年齢32.7歳)の16人の患者集団で検査した。

【0066】

ゲルの施与は、5-アミノレブリン酸の拡散のためのインキュベーション時間が単に90分であることを除いて、ローションに関する例3の記載と同様に行った。照射は、アルゴン-カラーレーザー(Coherent Innova, Modell 310, Palo Alto, CA)の使用下に、単色光(630nm)及び光用量 $50\text{ J/cm}^2 \sim 125\text{ J/cm}^2$ を用いて行った。

【0067】

1回の処置の後に、1～12ヶ月の再検査の間に16患者の9人で完全な消失及び他の7人は部分消失を示した。この処置は患者集団の大部分により良好に耐えられた。患者にとって、苦痛が過剰である場合には照射を中断することは自由であった。完全照射時間の達成までの中断の回数を確認した。患者の3人だけが5回以上頻繁に照射を中断し、5患者は照射を1回又は2回中断し、残りは中断を必要としなかった。

【手続補正書】特許協力条約第34条補正の翻訳文提出書

【提出日】平成12年12月22日(2000.12.22)

【手続補正1】

【補正対象書類名】明細書

【補正対象項目名】特許請求の範囲

【補正方法】変更

【補正内容】

【特許請求の範囲】

【請求項1】 5-アミノレブリン酸、その塩、錯体又は付加化合物及び／又はプロトポルフィリンIXに変換可能なその前駆物質及び／又は代謝産物から選択された作用物質及び担持剤を水相中に含むナノエマルジョンを含有し、その際、担持剤は脂質1種以上から及び大豆レシチンを含む乳化剤1種以上から形成されていることを特徴とする、組成物。

【請求項2】 乳化された粒子の平均寸法は10～200nmである、請求項1に記載の組成物。

【請求項3】 作用物質は、組成物の全質量に対して1～25質量%、殊に5～15質量%の配分で存在する、請求項1又は2に記載の組成物。

【請求項4】 更に、化粧品学又は製薬学で慣用である助剤及び／又は添加剤を含む、請求項1から3までのいずれか1項に記載の組成物。

【請求項5】 ゲルの形で存在し、組成物の全質量に対して作用物質5～15%、担持剤45～55%、助剤1～5%及び残りは水を含む、請求項4に記載の組成物。

【請求項6】 ローシヨンの形で存在し、組成物の全質量に対して作用物質5～15%、担持剤15～25%、助剤15～25%及び残りは水を含む、請求項4に記載の組成物。

【請求項7】 室温で1年貯蔵の後の作用物質の含分が5%より多くは減少していない、請求項1から6までのいずれか1項に記載の組成物。

【請求項8】 薬剤学的製剤の形である、請求項1から7までのいずれか1項に記載の組成物。

【請求項9】 局所適用可能である、請求項8に記載の組成物。

【請求項10】 請求項1から9までのいずれか1項に記載の組成物を製造する方法において、担持剤及び水相を含む混合物を製造し、ナノエマルジョンに変換し、その際、ナノエマルジョンに変換する前及び／又は後に作用物質を添加し、その後、場合により助剤及び／又は添加剤を加えて混合することを特徴とする、請求項1から9までのいずれか1項に記載の組成物の製法。

【請求項11】 酸素遮断下及び／又は光遮断下に操作する、請求項10に記載の方法。

【請求項12】 5～45℃の温度で操作する、請求項10又は11に記載の方法。

【請求項13】 光力学的治療用薬剤の製造のための、請求項1から9までのいずれか1項に記載の組成物の使用。

【請求項14】 組成物を局所的に適用する、請求項13に記載の使用。

【請求項15】 細胞増殖に結びついている疾病の治療用薬剤の製造のための、請求項13又は14に記載の使用。

【請求項16】 腫瘍疾病の治療用薬剤の製造のための、請求項15に記載の使用。

【請求項17】 疾病は、基底細胞癌、扁平上皮癌、ボウエン病、化学線角化症、尖圭コンジローム（CIN）、陰門の内皮腫瘍形成（VIN）又は瘤状又は皮下の癌疾病である、請求項16に記載の使用。

【請求項18】 疾病は乾癬である、請求項15に記載の使用。

【請求項19】 光力学的治療法において、請求項1から9までのいずれか1項に記載の組成物を罹病生体組織に有効量で適用し、処置すべき組織中に作用物質の十分な量を配量するために好適である時間インキュベートし、かつこの組織に光を照射することを特徴とする、光力学的治療法。

【請求項20】 増殖性細胞の検出のための、請求項1から9までのいずれか1項に記載の組成物の使用。

【請求項21】 腫瘍疾病の診断のための、請求項20に記載の使用。

【請求項22】 請求項9に記載の局所適用可能な組成物及び次のものから

選択された少なくとも1つの構成成分：

- (a) 実質的に光不透過性の枚葉状材料
- (b) この枚葉状材料を適用位置上に固定するための手段及び
- (c) 組成物を適用位置上に施与するための手段

を含むキット。

【国際調査報告】

INTERNATIONAL SEARCH REPORT

Int. Appl. No. PCT/EP 99/08711	
A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/107 A61K31/197 A61K41/00 A61P35/00 A61P17/06	
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 7 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 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.
X	HÜRLIMANN AF, ET AL.: "Photodynamic therapy of superficial basal cell carcinomas using topical 5-aminolevulinic acid in a nanocolloid lotion" DERMATOLOGY, vol. 197, no. 3, 1998, pages 248-254, XP000884929 ISSN 1018-8665 page 249, left-hand column, line 11 -page 250, left-hand column, line 15 table 2
	1,5, 9-11, 15-19, 21-23,25
X	EP 0 274 431 A (MEDAPHORE INC) 13 July 1988 (1988-07-13) page 16, line 58 -page 17, line 2 page 38, line 31 -page 39, line 16 claims 1,2,4,16,24-26; examples 129,133,135,140
	1,5,6, 9-14
-/--	
☒ 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	Date of mailing of the international search report
23 March 2000	29/03/2000
Name and mailing address of the ISA European Patent Office, P.O. Box 5010 Patentstrasse 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 551 apo.nl Fax (+31-70) 340-3016	Authorized officer Epskamp, S

Form PCT/ISA/210 (second sheet) (July 1992)

page 1 of 2

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/EP 99/08711

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 0 704 209 A (JOHNSON & JOHNSON MEDICAL) 3 April 1996 (1996-04-03) claims; examples ---	1-25
A	US 5 152 923 A (WEDER HANS G ET AL) 6 October 1992 (1992-10-06) cited in the application column 1, line 61 -column 4, line 15 claims; examples -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP99/08711

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:

Observation: Although claims 15-20 and 22 relate to a method for the treatment of the human or animal body, the search was carried out and was based on the cited effects of the compound/composition.
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 II Observations where unity of invention is lacking (Continuation of item 2 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 an additional fee, this Authority did not invite payment of any additional fee.
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.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP99/08711

ADDITIONAL MATTER

PCT/ISA/210

Continuation of Box I.1

Although claims 15-20 and 22 relate to a method for treatment of the human or animal body and although claim 23 relates to a diagnostic method that is conducted on the human or animal body, the search was carried out and was based on the cited effects of the composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No.

PCT/EP 99/08711

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0274431 A	13-07-1988	US 4794000 A	27-12-1988
		US 4914084 A	03-04-1990
		US 4963367 A	16-10-1990
		AT 105183 T	15-05-1994
		CA 1321542 A	24-08-1993
		DE 3889346 D	09-06-1994
		JP 63239213 A	05-10-1990
EP 0704209 A	03-04-1996	AU 3176695 A	04-04-1996
		BR 9504090 A	24-09-1996
		CA 2158724 A	21-03-1996
		JP 8175986 A	09-07-1996
US 5152923 A	06-10-1992	CH 677886 A	15-07-1991
		AT 94056 T	15-09-1993
		CA 2019710 A	26-12-1990
		DE 59082618 D	14-10-1993
		EP 0406162 A	02-01-1991
		JP 3047527 A	28-02-1991

Form PCT/ISA210 (patent family annex) (July 1992)

フロントページの続き

(51)Int.Cl. ⁷	識別記号	F I	キーワード (参考)
// A 6 1 N	5/06	A 6 1 N	5/06
(81)指定国	EP(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, I T, LU, MC, NL, PT, SE), OA(BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), AP(GH, GM, K E, LS, MW, SD, SL, SZ, TZ, UG, ZW), EA(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, C R, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, K Z, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, S K, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW		E
(71)出願人	Baarerstrasse 77, CH -6302 Zug, Switzerland		
(72)発明者	ゲルト ブルマイスター スイス国 ツンツゲン ノイマットシュト ラーセ 87		
F ターム(参考)	4C076 AA17 AA19 BB31 CC27 DD07 DD34 DD37 DD38 DD39 DD44 DD46 DD63F EE57F FF43 GG45 4C082 PA02 PC01 PC09 PE01 PL03 PL04 PL05 RA01 RA02 RC02 RE58 4C206 AA01 AA02 FA44 MA01 MA05 MA83 NA03 NA05 ZA89 ZB26		

PATENT TERM ADJUSTMENT STATEMENT UNDER 37 CFR 1.704(d)

Application Number	16/791,004
Filing Date	2/14/2020
First Named Inventor	Thomas BOYAJIAN
Art Unit	3792
Examiner Name	Tammie K. MARLEN
Practitioner Docket No.	067286-0410

APPLICANT HEREBY STATES THE FOLLOWING (please review 37 CFR 1.704(d) before filing this form):

☒ 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 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

AND/OR

☒ Each item of information contained in the information disclosure statement is a communication that was issued by a patent office in a counterpart foreign or international application or by the Office, and this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

INSTRUCTIONS:

- **This form will not satisfy the requirement of 37 CFR 1.97(e).** The present statement is filed under 37 CFR 1.704(d) and will not substitute for compliance with any of the requirements of 37 CFR 1.97 and 1.98. For an information disclosure statement to comply with 37 CFR 1.97(c) or (d), the information disclosure statement must be accompanied by a statement under 37 CFR 1.97(e) notwithstanding any statement filed under 37 CFR 1.704(d).
- The present form (PTO/SB/133) should be filed concurrently with the information disclosure statement to derive benefit under 37 CFR 1.704(d).

Signature	/Kiri Lee Sharon/	Date	15 Aug 2022
Typed or Printed Name	Kiri Lee Sharon	Practitioner Registration Number	71,828
<p>Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.</p>			
☒	*Total of <u>1</u> forms are submitted.		

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	16791004			
Filing Date:	14-Feb-2020			
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS			
First Named Inventor/Applicant Name:	Thomas Boyajian			
Filer:	Kiri Lee Sharon/Effie Hale			
Attorney Docket Number:	067286-0410			
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:				
UTILITY APPL ISSUE FEE	1501	1	1200	1200

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
Total in USD (\$)				1460

Electronic Acknowledgement Receipt

EFS ID:	46412092
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Kiri Lee Sharon/Effie Hale
Filer Authorized By:	Kiri Lee Sharon
Attorney Docket Number:	067286-0410
Receipt Date:	15-AUG-2022
Filing Date:	14-FEB-2020
Time Stamp:	15:31:53
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$ 1460
RAM confirmation Number	E20228EF34073395
Deposit Account	190741
Authorized User	Effie Hale

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

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	IssueFeeTrans.pdf	183183	no	1
			3531c1c961a1f10a2895bcf450b372fd41fe0989		
Warnings:					
Information:					
2	Miscellaneous Incoming Letter	Comments.pdf	113917	no	2
			f0423259bcbdb05a481481a9a6c0178e6b54e776		
Warnings:					
Information:					
3	Transmittal Letter	IDS_Trans.pdf	122576	no	3
			cdf7807e237525ffcf7710d1f9eb5e555321e57e		
Warnings:					
Information:					
4	Information Disclosure Statement (IDS) Form (SB08)	IDS_SB08.pdf	144437	no	1
			0caf672e6960b44a823c6d88932abf6d4f5c62a8		
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
5	Foreign Reference	JP2010_515714.pdf	1395629	no	26
			e1ac6af0b27571f013d0b7536102d0da195774f2		
Warnings:					
Information:					
6	Foreign Reference	JP-H04500770A.pdf	4092381	no	15
			a94dc7e278cdc1a5e1270051c528130ebabf6157		
Warnings:					

Information:					
7	Non Patent Literature	JP_OA_080222.pdf	1481364	no	6
			f54d2207a0c32271a3c761ede602a2db7913f963		
Warnings:					
Information:					
8	Foreign Reference	JP2002-529495.pdf	23425890	no	31
			bb8161ab27b413dc23826db9217b01ee8c575cfc		
Warnings:					
Information:					
9	Patent Term Adjustment Statement under 37 CFR 1.704(d) filed with an IDS	SB133.pdf	1052398	no	2
			a3c06d0f67b58b7824dae8825e1c4710b3a16395		
Warnings:					
Information:					
10	Fee Worksheet (SB06)	fee-info.pdf	40414	no	2
			3bc482c65dee9e10bdbe621eabf6811b538e7351		
Warnings:					
Information:					
Total Files Size (in bytes):			32052189		
<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>					

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

22428 7590 05/16/2022
FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631

TITLE OF INVENTION: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	08/16/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
MARLEN, TAMMIE K	3792	607-090000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Foley & Lardner LLP
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

DUSA PHARMACEUTICALS, INC.

(B) RESIDENCE: (CITY AND STATE OR COUNTRY)

Billerica, MA

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☒ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 19-0741

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

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.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Kiri Lee Sharon/

Date 15 Aug 2022

Typed or printed name Kiri Lee Sharon

Registration No. 71,828

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN

Title: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY
AND DIAGNOSIS

Appl. No.: 16/791,004

Filing Date: 2/14/2020

Examiner: Tammie K. MARLEN

Art Unit: 3792

Conf. No.: 2631

**RECORD OF INTERVIEW SUBSTANCE AND
COMMENTS ON REASONS FOR ALLOWANCE**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant sincerely appreciates the courtesy of the telephonic interview between Primary Examiner Marlen and the undersigned on May 17, 2022 in connection with the captioned application.

The PTO-issued interview summary issued May 20, 2022 is accurate.

Additionally, Applicant acknowledges the allowance of the captioned application with gratitude. Applicant wishes to thank the Examiner for the examination of the present application and for the allowance of the same.

To the extent that the Examiner's comments focus on specific claim language or find that the claims are patentable for specific reasons, Applicant respectfully responds that patentability should be assessed with reference to the claimed subject matter as a whole.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741.

Respectfully submitted,

Date: 15 Aug 2022

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4092
Facsimile: (202) 672-5399

By /Kiri Lee Sharon/

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN
Title: ADJUSTABLE ILLUMINATOR FOR
PHOTODYNAMIC THERAPY AND DIAGNOSIS
Application No.: 16/791,004
Filing Date: 2/14/2020
Examiner: Tammie K. MARLEN
Art Unit: 3792
Confirmation No.: 2631

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant submits herewith documents for the Examiner's consideration in accordance with 37 CFR §§1.56, 1.97 and 1.98.

Applicant respectfully requests that each listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The submission of any document herewith is not an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicant does not waive any rights to take any action, which would be appropriate to antedate or otherwise remove as a competent reference any document submitted herewith.

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(d), on or before payment of the issue fee.

CONCISE EXPLANATION OF RELEVANCE

Any document not in English and listed on the attached Form PTO/SB/08 has been cited in a communication in a corresponding non-U.S. application. An English abstract, English translation in full or in part, and/or an English-language counterpart is provided for each document not in English, as indicated on the Form PTO/SB/08 submitted herewith.

STATEMENT UNDER 37 CFR §1.704(d)

As to documents N5-N8, the undersigned hereby states in accordance with 37 CFR §1.704(d) that each item of information contained in this 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 that this communication was not received by any individual designated in 37 CFR §1.56(c) more than thirty days prior to the filing of the information disclosure statement; or is a communication that was issued by a patent office in a counterpart foreign or international application or by 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.

Documents N1-N4 are English-language counterparts provided to aid in review of listed documents which are not in English.

STATEMENT UNDER 37 CFR §1.97(e)

As to documents N5-N8, the undersigned hereby states in accordance with 37 CFR §1.97(e)(1) that each item of information contained in this information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three (3) months prior to filing of this statement.

As noted above, documents N1-N4 are English-language counterparts provided to aid in review of listed documents which are not in English.

FEES

Fees in the amount of \$260.00 to cover the fee associated with an information disclosure statement are being paid by credit card via EFS-Web.

The Commissioner is hereby authorized to charge any additional fees which may be required for this application to Deposit Account Number 19-0741.

Respectfully submitted,

Date 15 Aug 2022

By /Kiri Lee Sharon/

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4092
Facsimile: (202) 672-5399

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	08/24/2022		
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			08/24/2022	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):

ipdocketing@foley.com

Corrected Notice of Allowability	Application No. 16/791,004	Applicant(s) Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the IDS submitted on 8/15/2022.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ 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.

3. ☒ The allowed claim(s) is/are 1-6 and 11-24. As a result of the allowed claim(s), 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.

4. ☐ 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)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____ 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____ 4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____	5. ☐ Examiner's Amendment/Comment 6. ☐ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____
---	--

/TAMMIE K MARLEN/
 Primary Examiner, Art Unit 3792

Search Notes 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

CPC - Searched*		
Symbol	Date	Examiner
A61N 5/06,062,0616	10/20/2021	TKM
A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662	10/20/2021	TKM
A61B5/0064,0082	10/20/2021	TKM
Updated above	05/06/2022	TKM
Updated above	08/19/2022	TKM

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor name and assignee search	10/20/2021	TKM
Text-limited and related application search – see search history printout	10/20/2021	TKM
Consulted Alyssa Alter	10/20/2021	TKM
Updated above	05/06/2022	TKM
Updated above	08/19/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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<i>Search Notes</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	PGPUB text search -- see interference search printout	05/06/2022	TKM
	Updated above	08/19/2022	TKM

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
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Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	

CPC						
Symbol					Type	Version
A61N	/	5	/	062	F	2013-01-01
A61B	/	5	/	0064	I	2013-01-01
A61B	/	5	/	0082	I	2013-01-01
A61N	/	2005	/	0633	A	2013-01-01
A61N	/	2005	/	0626	A	2013-01-01
A61N	/	2005	/	0642	A	2013-01-01
A61N	/	2005	/	0652	A	2013-01-01
A61N	/	2005	/	0663	A	2013-01-01
A61N	/	2005	/	0662	A	2013-01-01
A61N	/	2005	/	0651	A	2013-01-01

CPC Combination Sets					
Symbol				Type	Set

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) 19 August 2022		O.G. Print Claim(s) 1	O.G. Print Figure 2A

<i>Issue Classification</i> 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.	
	Examiner TAMMIE K MARLEN	Art Unit 3792	

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61N5/06	/	5	/ 06
NON-CLAIMED			
/	/		

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	19 August 2022	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	2A

Issue Classification 	Application/Control No. 16/791,004	Applicant(s)/Patent Under Reexamination Boyajian et al.
	Examiner TAMMIE K MARLEN	Art Unit 3792

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1		10	17	19										
2	2	9	11	19	20										
3	3	12	12	6	21										
4	4	15	13	18	22										
5	5	10	14	7	23										
8	6	13	15	20	24										
	7	11	16												
	8	14	17												
	9	16	18												

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792 (Primary Examiner) _____ (Date) 19 August 2022		O.G. Print Claim(s) 1	O.G. Print Figure 2A

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	31	((("DUSA") near3 ("PHARMACEUTICALS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2019/03/25 10:32 AM
L2	30	((("BOYAJIAN") near3 ("Thomas")) OR ((("CAROTA") near3 ("Mark")) OR ((("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 10:32 AM
L3	6	("0000002" "0000003" "0000004" "0000005" "0000006" "0000007").PN	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L6	4	("0000001" "0000002" "0000003" "0000004").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L7	14	("0000001" "0000002" "0000003" "0000004" "20040162596" "20040260365" "5814008" "5849027" "9108045" "20050075703" "20060241726" "0000005" "0000006" "0000007").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 10:34 AM
L8	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 10:37 AM
L9	3	("0000002" "20050075703" "20060241726").PN	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 01:09 PM
L10	9	((("20030088296") or ("20050090877") or ("20060253175") or ("20070283655") or ("20100010591") or ("20110106222") or ("20140067024") or ("9533170")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 01:12 PM
L11	6	("0000002" "20040162596" "20040260365" "5814008" "5849027" "9108045").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 01:13 PM
L12	14	(US-0162109-\$ US-0287671-\$ US-0287696-\$ US-	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 01:16 PM

L13	3	20060287696-\$ US-20120287671-\$ US-20150162109-\$ US-7156865-\$).DID. (("20080031924") or ("20100174223") or ("20150238776")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 01:18 PM
L14	2	(("20160166846") or ("20130190845")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 01:19 PM
L15	12	"2007112427"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 02:58 PM
L16	5	"38541884".FMID.	(US-PGPUB; USPAT; FPRS)	OR	ON	ON	2019/03/25 02:58 PM
L17	8	"2011124912"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 02:59 PM
L18	4	"42228866".FMID.	(US-PGPUB; USPAT; FPRS)	OR	ON	ON	2019/03/25 03:00 PM
L19	6	("0000002" "0000003" "0000004" "0000005" "0000006" "0000007").PN	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM
L20	4	("0000001" "0000002" "0000003" "0000004").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM
L21	14	("0000001" "0000002" "0000003" "0000004" "20040162596" "20040260365" "5814008" "5849027" "9108045" "20050075703" "20060241726" "0000005" "0000006" "0000007").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM
L22	8	(US-6223071-\$ US-6709446-\$ US-7190109-\$ US-7723910-\$ US-8030836-\$ US-8216289-\$ US-8758418-\$).DID.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:01 PM
L23	3	("0000002" "20050075703" "20060241726").PN	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM
L24	9	(("20030088296") or ("20050090877") or ("20060253175") or ("20070283655") or ("20100010591") or ("20110106222") or ("20140067024") or ("9533170")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 03:01 PM
L25	6	("0000002" "20040162596" "20040260365" "58	(US-PGPUB; USPAT)	OR	ON	ON	2019/03/25 03:01 PM

L26	14	14008 "5849027 "9108045").PN. (US-0162109-\$ US-0287671-\$ US-0287696-\$ US-20060287696-\$ US-20120287671-\$ US-20150162109-\$ US-7156865-\$).DID.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:01 PM
L27	3	((("20080031924") or ("20100174223") or ("20150238776")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 03:01 PM
L28	2	((("20160166846") or ("20130190845")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/25 03:01 PM
L29	2008929	L19 a4 "s5" L20 L21 L22 L23 L24 L25 L26 L27 L28	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:01 PM
L30	50	L19 L20 L21 L22 L23 L24 L25 L26 L27 L28	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:02 PM
L31	6784	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L32	5	L16	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L33	11523	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L34	8633	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L35	2743	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L36	6725	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L37	572	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L38	1341	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L39	4107	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L40	1289	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:08 PM
L41	285	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM

L42	282	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM
L43	30801	L31 L33 L34 L35 L36 L37 L38 L39 L40 L41 L42	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:09 PM
L44	3652	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:10 PM
L45	31604	L43 L44	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:10 PM
L46	8642	L45 and (diode led)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:10 PM
L47	280	(L41 L37) and (L36 L39 L44 (diode led))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:18 PM
L48	280	(L41 L37) and (L36 L39 L44 (diode led))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:18 PM
L49	1828	L46 and (panel\$4 hing\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 03:19 PM
L50	21	(US-20180236259-\$ or US-20170007844-\$ or US-20150134032-\$ or US-20120265275-\$ or US-20140350644-\$ or US-20120150265-\$ or US-20180015297-\$ or US-20180193660-\$ or US-20180280718-\$ or US-20070016269-\$ or US-20180345034-\$ or US-20110054573-\$ or US-20100017953-\$ or US-20160129279-\$ or US-20170231058-\$ or US-20170238401-\$ or US-20160235980-\$ or US-20180133497-\$ or US-20180008839-\$).did. or (US-9950136-\$).did. or (WO-2018067411-\$).did.	(US-PGPUB; USPAT; FPRS)	OR	ON	ON	2019/03/25 03:35 PM
L51	21	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2019/03/25 04:11 PM

		US-20180345034-\$ or US-20180015297-\$).did. or (US-9533170-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.					
L52	17	L51 and (@ad<="20151015" @rlad<="20151015" @prad<="20151015")	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 04:12 PM
L53	4	L51 not L52	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/25 04:12 PM
L54	3	"39774377".FMID.	(US-PGPUB; USPAT; FPRS)	OR	ON	ON	2019/03/25 04:18 PM
L55	4	((("20050090877") or ("20060253175") or ("20140067024") or ("20060253175") or ("20150162109")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/29 08:51 AM
L56	6786	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L57	11526	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L58	8637	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L59	2747	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L60	6728	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L61	572	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L62	1341	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L63	4110	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L64	1289	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L65	285	A61N2005/064.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2019/03/29

L66	282	A61N2005/0658.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	08:56 AM 2019/03/29 08:56 AM
L67	30814	L56 L57 L58 L59 L60 L61 L62 L63 L64 L65 L66	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L68	3653	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L69	31617	L67 L68	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L70	2785	L69 and (panel\$4 hing\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:56 AM
L71	45	L69 and ((five fifth) with (panel\$4 hing\$6))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/03/29 08:58 AM
L72	1	("8021501").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2019/03/29 10:10 AM
L73	6919	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L74	11077	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L75	8626	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L76	2800	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L77	6742	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L78	578	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L79	1351	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L80	4117	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L81	1294	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L82	285	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM

L83	283	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L84	30469	L73 L74 L75 L76 L77 L78 L79 L80 L81 L82 L83	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L85	3612	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L86	31266	L84 L85	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L87	10	L86 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:24 AM
L88	618	L86 and ((sens\$6 determin\$6 detect\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/15 10:29 AM
L89	6941	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L90	11104	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L91	8674	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L92	2822	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L93	6752	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L94	581	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L95	1355	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L96	4132	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L97	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L98	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L99	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L100	30552	L89 L90 L91 L92 L93	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM

L101	3643	L94 L95 L96 L97 L98 L99 A61N2005/0662.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:34 PM 2019/10/31 01:34 PM
L102	31352	L100 L101	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L103	242	L102 and ((measur\$6) near3 (size shape))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/10/31 01:34 PM
L104	6943	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L105	11105	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L106	8678	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L107	2825	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L108	6754	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L109	583	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L110	1356	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L111	4135	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L112	1295	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L113	287	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L114	285	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L115	30563	L104 L105 L106 L107 L108 L109 L110 L111 L112 L113 L114	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L116	3643	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L117	31363	L115 L116	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2019/11/04 11:37 AM

L118	10	L117 and ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2019/11/04 11:37 AM
L124	1	("20120283328").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/01/31 08:26 AM
L125	22	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107- \$).did. or (US-9533170- \$).did. or (EP-2016977- \$ or WO-2018191356- \$).did. or (US- 20160175609-\$ or US- 20160175608-\$ or GB- 2501670-\$ or US- 20160175610-\$ or US- 20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/23 01:14 PM
L126	0	L125 and aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L127	0	L125 and ala	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 01:15 PM
L128	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L129	4618	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L130	2839	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L131	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L132	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L133	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L134	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM

L135	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L136	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:04 PM
L137	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L138	8097	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L139	13320	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L140	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L141	4119	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L142	8056	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L143	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L144	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L145	5508	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L146	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L147	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L148	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L149	36840	L138 L139 L140 L141 L142 L143 L144 L145 L146 L147 L148	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L150	4864	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L151	37870	L149 L150	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/23 03:05 PM
L152	46164	L128 L129 L130 L131	(US-PGPUB; USPAT;	OR	ON	ON	2020/11/23

L153	845	L132 L133 L134 L135 L136 L137 L151 L152 and \$2aminolevulinic	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:05 PM 2020/11/23 03:07 PM
L154	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L155	4619	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L156	2842	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L157	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L158	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L159	1645	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L160	5449	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L161	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L162	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L163	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L164	8098	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L165	13321	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L166	10819	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L167	4120	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L168	8057	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L169	733	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2020/11/24 06:15 AM

L170	1645	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L171	5509	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L172	1413	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L173	365	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L174	441	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L175	36843	L164 L165 L166 L167 L168 L169 L170 L171 L172 L173 L174	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L176	4865	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L177	37873	L175 L176	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L178	46171	L154 L155 L156 L157 L158 L159 L160 L161 L162 L163 L177	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L179	845	L178 and \$2aminolevulinic	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/24 06:15 AM
L180	1	(10/466734).APP.	(USPAT; USOCR)	OR	ON	ON	2020/11/24 01:51 PM
L181	12	"19912039".FMID.	(US-PGPUB; USPAT; FPRS; JPO)	OR	ON	ON	2020/11/24 01:58 PM
L182	39	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761" "20030088296" "20040162596" "20040260365" "20050075703" "20050090877" "20060241726" "20060253175" "20060287696" "20070283655" "20080031924" "20100010591" "20100174223" "20110106222" "20120283328" "20120287671" "20130066405" "20130190845" "20140067024" "20150162109" "20150238776" "20160166846" "20160175609" "5849	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/24 02:10 PM

L183	25	027" "6223071" "6709446" "7156865" "7190109" "7723910" "8030836" "8216289" "8758418" "9108045" "9533170").P N. (US-20070283655-\$ or US-20130066405-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$).did. or (US-9227082-\$ or US-9017391-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2020/11/27 01:52 PM
L184	56	(US-0010591-\$ US-0031924-\$ US-0066405-\$ US-0067024-\$ US-0075703-\$ US-0088296-\$ US-0090877-\$ US-0106222-\$ US-0162109-\$ US-0162596-\$ US-0166846-\$ US-0174223-\$ US-0175609-\$ US-0175610-\$ US-0190845-\$ US-0238776-\$ US-0241726-\$ US-0253175-\$ US-0260365-\$ US-0283328-\$ US-0283655-\$ US-0287671-\$ US-0287696-\$ US-16787667-\$ US-20030088296-\$ US-20040162596-\$ US-20040260365-\$ US-	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:55 PM

		20050075703-\$ US- 20050090877-\$ US- 20060241726-\$ US- 20060253175-\$ US- 20060287696-\$ US- 20070283655-\$ US- 20080031924-\$ US- 20100010591-\$ US- 20100174223-\$ US- 20110106222-\$ US- 20120283328-\$ US- 20120287671-\$ US- 20130066405-\$ US- 20130190845-\$ US- 20140067024-\$ US- 20150162109-\$ US- 20150238776-\$ US- 20160166846-\$ US- 20160175609-\$ US- 20160175610-\$ US- 5814008-\$ US- 5849027-\$ US- 6223071-\$ US- 6709446-\$ US- 7190109-\$ US- 7723910-\$ US- 8030836-\$ US- 8216289-\$ US- 8758418-\$ US- 9533170-\$).DID.					
L185	6	("0000001" "0000002" "20040010299" "20090324727" "20110053965" "20140010761").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2020/11/27 01:59 PM
L186	1	("10357567").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2020/11/27 01:59 PM
L187	18	L183 not (L184 L185 L186)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2020/11/27 01:59 PM
L188	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L189	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L190	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L191	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L192	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L193	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/16

L194	5775	A61N2005/0651.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:49 PM 2021/03/16 12:49 PM
L195	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L196	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L197	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L198	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L199	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L200	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L201	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L202	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L203	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L204	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L205	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L206	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L207	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L208	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L209	38191	L198 L199 L200 L201 L202 L203 L204 L205 L206 L207 L208	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L210	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/16 12:49 PM

L211	39273	L209 L210	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L212	47948	L188 L189 L190 L191 L192 L193 L194 L195 L196 L197 L211	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L213	987	L212 and hinge	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:49 PM
L214	23	L212 and (((wide\$4 and narrow\$6) or (first and second)) adj width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:50 PM
L215	117	L212 and (((wide\$4 and narrow\$6) or (first and second)) near3 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 12:51 PM
L216	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L217	4832	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L218	3002	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L219	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L220	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L221	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L222	5775	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L223	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L224	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L225	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L226	8407	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L227	13760	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM

L228	11191	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L229	4465	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L230	8317	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L231	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L232	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L233	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L234	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L235	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L236	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L237	38191	L226 L227 L228 L229 L230 L231 L232 L233 L234 L235 L236	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L238	5142	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L239	39273	L237 L238	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L240	47948	L216 L217 L218 L219 L220 L221 L222 L223 L224 L225 L239	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L241	199	L240 and (((wide\$4 and narrow\$6) or (first and second)) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/16 03:44 PM
L242	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L243	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L244	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L245	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/03/18

L246	757	A61N2005/0633.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	09:35 AM 2021/03/18 09:35 AM
L247	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L248	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L249	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L250	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L251	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L252	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L253	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L254	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L255	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L256	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L257	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L258	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L259	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L260	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L261	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L262	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO;	OR	ON	ON	2021/03/18 09:35 AM

L263	38197	L252 L253 L254 L255 L256 L257 L258 L259 L260 L261 L262	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L264	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L265	39279	L263 L264	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L266	47959	L242 L243 L244 L245 L246 L247 L248 L249 L250 L251 L265	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L267	199	L266 and (((wide\$4 and narrow\$6) or (first and second)) near6 width)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 09:35 AM
L268	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L269	4833	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L270	3005	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L271	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L272	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L273	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L274	5776	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L275	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L276	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L277	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L278	8408	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L279	13763	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM

L280	11195	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L281	4468	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L282	8318	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L283	757	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L284	1715	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L285	5842	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L286	1441	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L287	391	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L288	463	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L289	38197	L278 L279 L280 L281 L282 L283 L284 L285 L286 L287 L288	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L290	5144	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L291	39279	L289 L290	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L292	47959	L268 L269 L270 L271 L272 L273 L274 L275 L276 L277 L291	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/03/18 08:28 PM
L293	0	2007/112427	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:22 PM
L294	582470	(stephen tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L295	242	(stephen and tobin).in.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 01:23 PM
L296	10	("0000001" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM

L297	2	("5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L298	3	("0000002" "D000001").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:13 PM
L299	10	("5032400" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20160045757" "5601838" "5686065" "6897238").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:14 PM
L300	1	("20110224598").PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	2021/07/07 03:15 PM
L301	3	("0000001" "7033381" "7730893").PN.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 03:16 PM
L302	14	L299 L300 L301	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:16 PM
L303	9	L302 and (wid\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:18 PM
L304	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L305	4963	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L306	3093	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L307	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L308	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L309	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L310	5920	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L311	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L312	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L313	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM

L314	8498	A61N5/06.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L315	13949	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L316	11425	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L317	4694	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L318	8474	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L319	785	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L320	1739	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L321	6023	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L322	1468	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L323	399	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L324	469	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L325	38854	L314 L315 L316 L317 L318 L319 L320 L321 L322 L323 L324	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L326	5338	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L327	39953	L325 L326	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L328	48853	L304 L305 L306 L307 L308 L309 L310 L311 L312 L313 L327	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:19 PM
L329	217	L328 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/07/07 03:21 PM
L331	3	("0000001" "0000002" "	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26

L332	2	20200100997").PN. (("20160346392") or ("20200100997")).PN.	(US-PGPUB; USPAT; USOCR; EPO; JPO)	OR	OFF	OFF	12:36 PM
L333	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:37 PM
L334	5141	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L335	3204	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L336	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L337	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L338	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L339	6128	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L340	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L341	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L342	6224	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L343	8694	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L344	14216	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L345	11742	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L346	4914	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L347	8649	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L348	808	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L349	1778	A61N2005/0642.cpc.	(US-PGPUB; USPAT;	OR	ON	ON	2021/08/26

L350	6224	A61N2005/0663.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	12:42 PM 2021/08/26 12:42 PM
L351	1481	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L352	408	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L353	492	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L354	39744	L343 L344 L345 L346 L347 L348 L349 L350 L351 L352 L353	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L355	5526	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L356	40873	L354 L355	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L357	50063	L333 L334 L335 L336 L337 L338 L339 L340 L341 L342 L356	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L358	222	L357 and (((wide\$4 and narrow\$6) or (first and second)) near6 width) or ((wide\$6 and narrow\$6) near6 panel))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/08/26 12:42 PM
L360	37	((("DUSA") near3 ("PHARMACEUTICALS ") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2021/10/18 03:52 PM
L361	38	((("BOYAJIAN") near3 ("Thomas")) OR (("CAROTA") near3 ("Mark")) OR (("MAZEJKA") near3 ("Brian"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:52 PM
L362	64	("0000002" "0000011" "20200100997" "0000001" "20190290763" "20200269063" "20200398071" "7730893" "20090247932" "20110224598" "20130274834" "20130289089" "20150290028" "20160008623" "20200261580" "20100298758" "20110020441" "20110293528" "20130304019" "20130315999" "20	(US-PGPUB; USPAT)	OR	ON	ON	2021/10/18 03:52 PM

		160045757" "5601838" "5686065" "6897238" "0 017109" "20010021812 " "D000001" "20040010 299" "20090324727" "2 0110053965" "2014001 0761" "20030088296" " 20040162596" "200402 60365" "20050075703" " "20050090877" "20060 241726" "20060253175 " "20060287696" "2007 0283655" "2008003192 4" "20100010591" "201 00174223" "201101062 22" "20120283328" "20 120287671" "20130066 405" "20130190845" "2 0140067024" "2015016 2109" "20150238776" " 20160166846" "201601 75609" "5849027" "622 3071" "6709446" "7156 865" "7190109" "77239 10" "8030836" "821628 9" "8758418" "9108045" "9533170").PN.					
L363	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L364	5189	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L365	3246	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L366	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L367	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L368	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L369	6171	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L370	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L371	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L372	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18

L373	8738	A61N5/06.cpc.	USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	03:53 PM
L374	14281	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L375	11844	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L376	4993	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L377	8713	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L378	815	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L379	1794	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L380	6285	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L381	1484	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L382	413	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L383	498	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L384	39984	L373 L374 L375 L376 L377 L378 L379 L380 L381 L382 L383	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L385	5588	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L386	41124	L384 L385	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L387	50408	L363 L364 L365 L366 L367 L368 L369 L370 L371 L372 L386	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L388	3097	L387 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:53 PM
L389	29	(US-20070283655-\$ or US-20130066405-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM

		US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$).did.					
L390	10	L389 and (uniform\$6 with (light illuminat\$8))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/18 03:54 PM
L391	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L392	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L393	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L394	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L395	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L396	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L397	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L398	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L399	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM

L400	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L401	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L402	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L403	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L404	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L405	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L406	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L407	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L408	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L409	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L410	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L411	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L412	40271	L401 L402 L403 L404 L405 L406 L407 L408 L409 L410 L411	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L413	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L414	41417	L412 L413	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L415	50819	L391 L392 L393 L394 L395 L396 L397 L398 L399 L400 L414	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L416	15	L415 and (nest\$6 near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:27 AM
L417	7	L415 and (recess\$6	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/19

		near3 hing\$9)	USOCR; FPRS; EPO; JPO; DERWENT)				10:30 AM
L418	0	L415 and (hidden near3 hing\$9)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 10:30 AM
L419	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L420	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L421	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L422	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L423	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L424	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L425	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L426	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L427	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L428	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L429	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L430	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L431	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L432	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L433	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L434	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM

L435	1805	A61N2005/0642.cpc.	JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L436	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L437	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L438	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L439	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L440	40271	L429 L430 L431 L432 L433 L434 L435 L436 L437 L438 L439	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L441	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L442	41417	L440 L441	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L443	50819	L419 L420 L421 L422 L423 L424 L425 L426 L427 L428 L442	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L444	59	L443 and (dead near3 space)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:50 PM
L445	61	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:51 PM
L446	66	L443 and (hing\$6 with (reduce reduced reducing reduction minim\$9 decreas\$6))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L447	112	L444 L445 L446	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/19 03:52 PM
L448	30	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM

		US-20180093107-\$ or US-20010021812-\$ or US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L449	17	L448 and output	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:42 PM
L450	19	L448 and (shape size measur\$6)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:45 PM
L451	14390	A61N5/062.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L452	5241	A61B5/0064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L453	3302	A61B5/0082.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L454	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L455	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L456	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L457	6249	A61N2005/0651.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L458	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L459	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L460	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L461	8783	A61N5/06.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM

L462	14390	A61N5/062.cpc.	USOCR; FPRS; EPO; JPO; DERWENT) (US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	01:49 PM 2021/10/20 01:49 PM
L463	11938	A61N5/0616.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L464	5080	A61N2005/0626.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L465	8785	A61N2005/0652.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L466	826	A61N2005/0633.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L467	1805	A61N2005/0642.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L468	6340	A61N2005/0663.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L469	1489	A61N2005/0636.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L470	416	A61N2005/064.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L471	512	A61N2005/0658.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L472	40271	L461 L462 L463 L464 L465 L466 L467 L468 L469 L470 L471	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L473	5664	A61N2005/0662.cpc.	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L474	41417	L472 L473	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L475	50819	L451 L452 L453 L454 L455 L456 L457 L458 L459 L460 L474	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L476	1292	L475 and ((sens\$6 detect\$6) near5 (shape size))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:49 PM
L477	45	L475 and ((sens\$6 detect\$6) with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:51 PM
L478	54	L475 and ((sens\$6	(US-PGPUB; USPAT;	OR	ON	ON	2021/10/20

		detect\$6 measur\$6) with (shape size) with (treatment adj (surface area)))	USOCR; FPRS; EPO; JPO; DERWENT)				01:54 PM
L479	162	L475 and ((sens\$6 detect\$6 measur\$6 adjust adjusting adjusted adjustable "based on") with (shape size) with (treatment adj (surface area)))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:58 PM
L480	88	L479 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 01:59 PM
L481	17	L448 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L482	0	L448 and ("j/cm" "mw/cm")	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:47 PM
L483	7	L475 and ("j/cm" "mw/cm" nm nanometer)	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:47 PM
L484	46	L475 and ("j/cm" "mw/cm" (nm or nanometer))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	AND	ON	ON	2021/10/20 03:48 PM
L485	34	L484 and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:48 PM
L486	629	L475 and (intensity with red) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L487	442	L475 and (intensity with red with light) and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:52 PM
L488	0	L475 and (intensity with red with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L489	7	L475 and (intensity with "j/cm") and @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2021/10/20 03:53 PM
L490	32	(US-20070283655-\$ or US-20130066405-\$ or US-20120287671-\$ or US-20060241726-\$ or US-20160175609-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20170131693-\$ or US-20170007844-\$ or US-20180345034-\$ or US-20180015297-\$ or US-20180093107-\$ or US-20010021812-\$ or	(US-PGPUB; USPAT; FPRS; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM

		US-20050075703-\$ or US-20160310756-\$ or US-20130190845-\$ or US-20130066404-\$ or US-20030216795-\$).did. or (US-9533170-\$ or US-9227082-\$ or US-9017391-\$ or US-4100415-\$).did. or (EP-2016977-\$ or WO-2018191356-\$).did. or (US-20160175609-\$ or US-20160175608-\$ or GB-2501670-\$ or US-20160175610-\$ or US-20140157511-\$ or US-20160310756-\$).did.					
L491	20	L490 and intensity	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT)	OR	ON	ON	2022/01/24 10:45 AM
L492	3	("0000002" OR "0017487" OR "0017506").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L493	2	("0000001" OR "0000002").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L494	3	("0000001" OR "0000002" OR "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:09 AM
L495	3	("11135293" "20100174222" "20150290470").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/03/23 11:17 AM
L496	53969	A61N5/062,06,0616.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:37 PM
L497	40946	A61N2005/0626,0652,0633,0642,0663,0636,064,0658,0651,0662.cpc.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL,	OR	ON	ON	2022/03/23 03:38 PM

L498	13206	A61B5/0064,0082.cpc.	NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L499	85960	496 497 498	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:38 PM
L500	20151	499 AND (intensity WITH light)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:39 PM
L501	7575	499 AND (intensity WITH light WITH (more	(US-PGPUB; USPAT; USOCR; FIT (AP, AT,	OR	ON	ON	2022/03/23 03:40 PM

		less higher lower highest lowest greater))	AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L502	2876	499 AND (intensity WITH light WITH (more less higher lower highest lowest greater))	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:47 PM
L503	4680	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L504	1777	502 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; IBM_TDB)	OR	ON	ON	2022/03/23 03:48 PM
L505	4689	501 AND @ad<="20151015"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:25 PM
L508	408	L505 AND hing\$6	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY,	OR	ON	ON	2022/05/06 02:47 PM

L509	116	((US-20130190845-A1 OR US-20120148975-A1 OR US-20130196284-A1 OR US-20120148976-A1 OR US-20100179622-A1 OR US-20130280671-A1 OR US-20140072932-A1 OR US-20050004632-A1 OR US-20070248930-A1 OR US-20150140502-A1 OR US-20110176326-A1 OR US-20070129776-A1 OR US-20020035386-A1 OR US-20020120312-A1 OR US-20070283655-A1 OR US-20120150265-A1 OR US-20160129279-A1 OR US-20140277291-A1 OR US-20130303972-A1 OR US-20020029071-A1 OR US-20070150031-A1 OR US-20130079759-A1 OR US-20130178919-A1 OR US-20160158485-A1 OR US-20160175609-A1 OR US-20100030013-A1 OR US-20090054953-A1 OR US-20040249423-A1 OR US-20160101295-A1 OR US-20030004499-A1 OR US-20120330386-A1 OR US-20090005839-A1 OR US-20140187998-A1 OR US-20160325109-A1	CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); USPAT; DERWENT)	OR	ON	ON	2022/05/06 02:53 PM
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		OR US-20060241726-A1 OR US-20140100455-A1 OR US-20050075703-A1 OR US-20050234383-A1 OR US-20100100160-A1 OR US-20050237423-A1 OR US-20110178582-A1 OR US-20060064144-A1 OR US-20010021812-A1 OR US-20140315142-A1 OR US-20050131500-A1 OR US-20060007390-A1 OR US-20080269730-A1 OR US-20120203310-A1 OR US-20120215291-A1 OR US-20160096042-A1 OR US-20110290005-A1 OR US-20060047329-A1 OR US-20090005837-A1 OR US-20160066791-A1 OR US-20140060546-A1 OR US-20080027317-A1 OR US-20170238401-A1 OR US-20170105265-A1 OR US-20100211136-A1 OR US-20170231058-A1 OR US-20080245371-A1 OR US-20140350395-A1 OR US-20150265366-A1).did. AND PGPB.dbnm.) OR ((DE-102015107669-A1 OR KR-20150126087-A OR CN-88102683-A OR KR-20140058327-A OR KR-101350503-B1 OR WO-2015041919-A1 OR WO-2006028465-A1 OR DE-202012004264-U1 OR FR-2931685-A1 OR CN-102300605-A OR WO-2012086991-A2 OR DE-202006017153-U1 OR DK-201500153-A1 OR CN-102300606-A OR CN-102481456-A OR WO-9614792-A1 OR KR-20160041129-A					
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		OR KR-20150124016-A OR CA-2638508-A1 OR RU-2483764-C2 OR KR-20120036564-A OR KR-20020088833-A OR EP-2502647-A1 OR CN-103930162-A OR EP-1839703-A1 OR FR-2601784-A1 OR CN-104640602-A OR DE-4015406-A1 OR WO-2014102791-A2 OR CA-2771517-A1 OR KR-20080094715-A OR EP-2749317-A1 OR CN-1039119-A OR CN- 1602172-A OR CN- 102883776-A OR WO- 2014080103-A2 OR CN-105380745-B OR DE-102007018863-A1 OR CA-2551311-A1 OR DE-10326522-A1 OR GB-2415387-A OR CN- 101646924-A OR DE- 202007005751-U1 OR CN-1708261-A OR CN- 104602638-A).did. AND FTDB.dbnm.) OR ((US- 4612604-A OR US- 4848323-A OR US- 7033381-B1 OR US- 8170657-B1 OR US- 9808644-B2 OR US- 10052393-B2 OR US- 10194808-B1).did. AND USPT.dbnm.) OR ((WO-2012075584- A1).did. AND DWPI.dbnm.)					
L510	408	((US-20130190845-A1 OR US-20120148975- A1 OR US- 20130196284-A1 OR US-20120148976-A1 OR US-20100179622- A1 OR US- 20130280671-A1 OR US-20140072932-A1 OR US-20050004632- A1 OR US- 20070248930-A1 OR US-20100318161-A1 OR US-20130253620- A1 OR US- 20140121731-A1 OR US-20150079536-A1 OR US-20150140502-	(US-PGPUB; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); USPAT; DERWENT)	OR	ON	ON	2022/05/06 02:55 PM

		A1 OR US- 20110176326-A1 OR US-20070129776-A1 OR US-20020035386- A1 OR US- 20020120312-A1 OR US-20070283655-A1 OR US-20120150265- A1 OR US- 20160129279-A1 OR US-20140277291-A1 OR US-20130303972- A1 OR US- 20020029071-A1 OR US-20040127961-A1 OR US-20070233209- A1 OR US- 20070150031-A1 OR US-20130079759-A1 OR US-20130178919- A1 OR US- 20160158485-A1 OR US-20160175609-A1 OR US-20100030013- A1 OR US- 20090054953-A1 OR US-20040249423-A1 OR US-20060009822- A1 OR US- 20160101295-A1 OR US-20030004499-A1 OR US-20120330386- A1 OR US- 20090005839-A1 OR US-20140187998-A1 OR US-20160325109- A1 OR US- 20060241726-A1 OR US-20070038269-A1 OR US-20140100455- A1 OR US- 20170035299-A9 OR US-20050075703-A1 OR US-20050234383- A1 OR US- 20070129778-A1 OR US-20100100160-A1 OR US-20050237423- A1 OR US- 20080079802-A1 OR US-20110178582-A1 OR US-20060064144- A1 OR US- 20010021812-A1 OR US-20040143308-A1 OR US-20140315142- A1 OR US- 20050131500-A1 OR					
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		US-20060007390-A1 OR US-20080269730-A1 OR US-20120203310-A1 OR US-20130253619-A1 OR US-20120215291-A1 OR US-20160096042-A1 OR US-20110290005-A1 OR US-20130152670-A1 OR US-20130179120-A1 OR US-20130184846-A1 OR US-20130182882-A1 OR US-20130191084-A1 OR US-20130197888-A1 OR US-20060047329-A1 OR US-20100076526-A1 OR US-20090005837-A1 OR US-20160066791-A1 OR US-20140060546-A1 OR US-20080027317-A1 OR US-20080045841-A1 OR US-20080287806-A1 OR US-20130123640-A1 OR US-20140194751-A1 OR US-20150080745-A1 OR US-20170238401-A1 OR US-20170105265-A1 OR US-20100211136-A1 OR US-20170231058-A1 OR US-20080245371-A1 OR US-20140107404-A1 OR US-20140350395-A1 OR US-20150265366-A1 OR US-20150265353-A1).did. AND PGPB.dbnm.) OR ((WO-2010142031-A1 OR WO-2010142013-A1 OR KR-20120047227-A OR JP-2012529299-A OR CN-102802726-A OR JP-5705838-B2 OR KR-101670537-B1 OR CN-102802726-B OR WO-2012048423-A1 OR EP-2627283-B1 OR DE-102015107669-A1 OR WO-2012075584-					
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		A1 OR EP-2648651-B1 OR WO-2009004412- A1 OR CN-101687099- A OR EP-2164566-B1 OR CN-101687099-B OR KR-20150126087-A OR CN-88102683-A OR DE-3814611-A1 OR NL-8801071-A OR IT- 1217200-B OR WO- 2013155632-A1 OR CN-104379087-A OR JP-2015515333-A OR JP-6007313-B2 OR CN-104379087-B OR CN-106621060-A OR EP-2838468-B1 OR EP-3263066-A1 OR CN-106621060-B OR EP-3626206-A1 OR KR-20140058327-A OR KR-101350503-B1 OR WO-2015041919-A1 OR WO-2015058284- A1 OR CN-105682603- A OR JP-2016538028- A OR JP-6484235-B2 OR CN-111330163-A OR EP-3845200-A1 OR WO-2011082420-A1 OR WO-2006028465- A1 OR CA-2579639-A1 OR DE-202012004264- U1 OR FR-2931685-A1 OR CN-102300605-A OR WO-2007047892- A1 OR CA-2343843-A1 OR GB-2361430-A OR EP-1147785-A2 OR JP- 2002102364-A OR WO- 2012086991-A2 OR KR-20120069588-A OR KR-20140072854-A OR KR-101845073-B1 OR DE-202006017153-U1 OR DE-102006008774- A1 OR WO- 2007098883-A2 OR CA-2373594-C OR CA- 2706642-C OR WO- 2007112427-A2 OR CA-2664898-A1 OR WO-2012082739-A2 OR EP-0148144-A2 OR HU-189454-B OR SE- 455837-B OR FI-79470- B OR FI-79470-C OR WO-2016007798-A2					
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		OR DK-201500153-A1 OR DK-178588-B1 OR CN-102300606-A OR CA-2846344-A1 OR EP-2778752-A2 OR KR-20140113561-A OR JP-2014180565-A OR AU-2014201546-A1 OR SG-10201400483T-A OR BR-102014006370- A2 OR EP-2778752-B1 OR TW-I576092-B OR RU-2661020-C2 OR JP-6362885-B2 OR WO-2012176071-A2 OR CN-102481456-A OR JP-2012532643-A OR WO-9614792-A1 OR CN-1164180-A OR CN-1124822-C OR CA- 2672092-A1 OR CA- 2341951-A1 OR GB- 2360461-A OR GB- 2360460-A OR EP- 1138349-A2 OR JP- 2002065875-A OR EP- 1457234-A2 OR JP- 2005334670-A OR EP- 1457234-B1 OR JP- 4889247-B2 OR WO- 2007000059-A1 OR CA-2613973-A1 OR CN-101242871-A OR KR-20160041129-A OR KR-101642839-B1 OR NL-8700329-A OR EP- 0283062-A2 OR EP- 0283062-B1 OR WO- 2012010861-A1 OR CA-2842275-A1 OR NZ-607470-A OR KR- 20150124016-A OR WO-2012040854-A1 OR CA-2812302-A1 OR CN-103237574-A OR JP-2013541977-A OR CA-2638508-A1 OR WO-2010015080-A1 OR CN-102143731-A OR RU-2483764-C2 OR WO-2006013390- A1 OR GB-2425481-A OR JP-2008508918-A OR EP-1824561-B1 OR WO-2004110305-A2 OR JP-2007526003-A OR WO-03001984-A2 OR KR-20040048881-A					
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		OR CN-1578688-A OR JP-2005521432-A OR AU-2002320215-B2 OR CA-2452408-C OR CN- 1578688-B OR KR- 20120036564-A OR KR-101181054-B1 OR KR-20020088833-A OR KR-100848391-B1 OR WO-2011067603-A1 OR CA-2782496-A1 OR AU-2010326393-A1 OR CN-102711912-A OR WO-2007040691-A1 OR CA-2624668-A1 OR WO-2012174245-A1 OR WO-2015006872- A1 OR WO- 2004075985-A2 OR WO-2004075984-A1 OR JP-2006519047-A OR JP-2011098207-A OR WO-02062420-A1 OR EP-1359977-B1 OR DE-60207202-T2 OR NO-331280-B1 OR WO-9919024-A1 OR EP-1021223-B1 OR DE-69827286-T2 OR JP-4257718-B2 OR CA- 2304774-C OR WO- 2010044879-A2 OR CA-2777481-A1 OR JP- 2012505706-A OR WO- 2006122229-A2 OR CA-2605346-A1 OR AU-2006243966-A1 OR JP-2008541092-A OR EP-1889470-B1 OR EP-2975834-A1 OR GB-2461806-A OR WO-2010007419-A1 OR EP-2339999-B1 OR WO-2006012123-A2 OR EP-2502647-A1 OR WO-2005049127-A1 OR AU-2004291100-A1 OR JP-2007511286-A OR CN-103930162-A OR EP-1839703-A1 OR WO-2012106541-A1 OR CA-2826245-A1 OR CN-103338818-A OR KR-20140044302-A OR EP-2670481-B1 OR DK-2670481-T3 OR RU-2600223-C2 OR CN-103338818-B OR					
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		<p> TW-I603754-B OR KR-101842423-B1 OR FR-2601784-A1 OR EP-0255426-A1 OR WO-2012106542-A1 OR CA-2826247-A1 OR KR-20140044300-A OR EP-2670482-B1 OR RU-2580983-C2 OR TW-I598127-B OR KR-101834155-B1 OR CN-104640602-A OR CN-104640602-B OR DE-4015406-A1 OR WO-2014102791-A2 OR WO-2016057729-A1 OR JP-2017534373-A OR CN-107427407-A OR JP-6608440-B2 OR CN-107427407-B OR CA-2771517-A1 OR KR-20080094715-A OR CN-101495182-A OR KR-101370160-B1 OR WO-2013002935-A1 OR CA-2840434-A1 OR JP-2014526166-A OR CA-2840434-C OR EP-2749317-A1 OR CN-1039119-A OR CN-1602172-A OR CA-2465906-C OR CN-102883776-A OR WO-2014080103-A2 OR EP-2922518-B1 OR ES-2828000-T3 OR CN-105380745-B OR DE-102007018863-A1 OR DE-102007018863-B4 OR CA-2551311-A1 OR DE-10326522-A1 OR EP-1486186-B1 OR WO-2008094252-A2 OR CA-2677217-A1 OR CA-2677217-C OR GB-2415387-A OR CA-2570919-A1 OR AU-2005256804-A1 OR KR-20070052742-A OR CN-1988932-A OR EP-1771225-B1 OR ES-2385991-T3 OR CN-101646924-A OR WO-2013112856-A2 OR EP-2807111-B1 OR WO-2015113003-A1 OR WO-2015184019-A1 OR DE- </p>					
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		202007005751-U1 OR EP-2489402-A2 OR EP-2489401-A2 OR EP-2489400-A2 OR WO-2016022612-A1 OR CN-1708261-A OR WO-2008124641-A2 OR CA-2858610-A1 OR CN-104080400-A OR EP-3466335-A1 OR BR-112014014781-A2 OR WO-2015143026- A1 OR CN-104602638- A OR CN-104602638-B OR CN-108113762- A).did. AND FTDB.dbnm.) OR ((US- 9242118-B2 OR US- 9463333-B2 OR US- 8900282-B2 OR US- 9308389-B2 OR US- 9730780-B2 OR US- 8702291-B2 OR US- 6626932-B2 OR US- 6796994-B2 OR US- 7517101-B2 OR US- 8425577-B2 OR US- 4612604-A OR US- 9289623-B2 OR US- 8980174-B2 OR US- 6645230-B2 OR US- 4848323-A OR US- 9533170-B2 OR US- 8070669-B2 OR US- 7033381-B1 OR US- 9138595-B2 OR US- 10252079-B2 OR US- 10342991-B2 OR US- 8170657-B1 OR US- 9808644-B2 OR US- 6663659-B2 OR US- 9854977-B2 OR US- 7311722-B2 OR US- 7730893-B2 OR US- 7298415-B2 OR US- 8279334-B2 OR US- 9079021-B2 OR US- 6223071-B1 OR US- 9320580-B2 OR US- 7449026-B2 OR US- 7147319-B2 OR US- 10384070-B2 OR US- 9248309-B2 OR US- 10667990-B2 OR US- 8384916-B2 OR US- 8493574-B2 OR US- 8743377-B2 OR US- 8874404-B2 OR US-					
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L511	408	<p>9013701-B2 OR US-9175945-B2 OR US-9448061-B2 OR US-7544204-B2 OR US-10238294-B2 OR US-9907688-B2 OR US-8380291-B2 OR US-8391960-B2 OR US-8706200-B2 OR US-8838210-B2 OR US-9186063-B2 OR US-9226664-B2 OR US-10052393-B2 OR US-10357662-B2 OR US-10194808-B1 OR US-8528563-B2 OR US-9301770-B2 OR US-10165976-B2 OR US-9700342-B2).did. AND USPT.dbnm.) OR ((WO-2012075584-A1).did. AND DWPI.dbnm.)</p> <p>L510 AND (intensity WITH light WITH (more less higher lower highest lowest greater))</p>	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/05/06 02:55 PM
L512	5	("0000001" OR "0000002" OR "20160030565" OR "5211938" OR "6559183").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:04 PM
L513	1	kennedy.in. AND @pd="19970708"	(US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:05 PM
L514	1	("5211938").pn.	(US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:07 PM
L515	1	("5211938").pn.	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2022/08/19 12:07 PM
L516	5	("5211938").pn.	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB,	OR	ON	ON	2022/08/19 12:07 PM

L517	1	5211938b1	HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB) (US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/08/19 12:07 PM
L518	0	"5211938-b1"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/08/19 12:08 PM
L519	1	"5211938 b1"	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/08/19 12:08 PM

L520	2545	@pd="19970708"	IBM_TDB) (US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:09 PM
L521	16	@pd="19970708" AND kennedy	(US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:09 PM
L522	0	kennedy.in. AND @pd="19970807"	(US-PGPUB; USPAT)	OR	ON	ON	2022/08/19 12:11 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N119	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:19 AM
N120	882	(panel AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:20 AM
N121	189	(panel AND width AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N122	213	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((sens\$6 determin\$6 detect\$6 measur\$6) near3 (size shape))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:23 AM
N123	3	(panel AND (width wide wider) AND (light illuminat\$6 led) AND ((nest\$6 near3 hing\$6) (optical\$6 near3 dead))).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2019/11/04 11:38 AM
N330	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/07/07 07:14 PM
N359	15	(panel AND (width wide wider) AND (light illuminat\$6 led) AND (ala aminolevul\$8)).clm.	(US-PGPUB; USPAT)	OR	ON	ON	2021/08/26 12:42 PM
N361	3	(panel AND (width wide wider longer long short shorter bigger) AND	(US-PGPUB; USPAT)	OR	ON	ON	2022/05/06 02:49 PM

		((light illuminat\$6 led) WITH intens\$6) AND (nest\$6 WITH hing\$6)).clm.					
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PTO/SB/08 (modified)

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT Date Submitted: August 15, 2022 <i>(use as many sheets as necessary)</i>				Complete if Known	
				Application Number	16/791,004
				Filing Date	2/14/2020
				First Named Inventor	Thomas BOYAJIAN
				Art Unit	3792
Examiner Name	Tammie K. MARLEN				
Attorney Docket Number	067286-0410				
Sheet	1	of	1		

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	N1	5,211,938	05-18-1993	KENNEDY ET AL.	
	N2	5,211,938-B1	07-08-1997	KENNEDY ET AL.	
	N3	6,559,183-B1	05-06-2003	SCHMID ET AL.	
	N4	2016/0030565-A1	02-04-2016	WULF ET AL.	

UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS					
Examiner Initials*	Cite No. ¹	U.S. Patent Application Document Serial Number-Kind Code ² (if known)	Filing Date of Cited Document MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Documents	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	N5	JP-2002-529495-A	09-10-2002	ASAT AG APPLIED SCIENCE & TECHNOLOGY		ABS, =N3
	N6	JP-2010-515714-A	05-13-2010	PHOTOCURE ASA		ABS, =N4
	N7	JP-H04-500770-A	02-13-1992	QUEENS UNIVERSITY		√, = N1, N2

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 ⁶
	N8	Japanese Office Action and English Translation, Application No. JP 2020-503004, Dated 8/2/2022 (6 pages)	√

Examiner Signature	/TAMMIE K MARLEN/	Date Considered	08/19/2022
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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	09/20/2022	11446512	067286-0410	2631

22428 7590 08/31/2022

FOLEY & LARDNER LLP
3000 K STREET N.W.
SUITE 600
WASHINGTON, DC 20007-5109

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 5 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional inventors):

Thomas Boyajian, Wilmington, MA;
Mark Carota, Chelmsford, MA;
Brian Mazejka, Salem, NH;

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

DUSA Pharmaceuticals, Inc., Wilmington, MA;

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 USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.



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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	09/07/2022		
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			09/07/2022	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):

ipdocketing@foley.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 16/791,004	Applicant(s) Boyajian et al.		
	Examiner TAMMIE K MARLEN	Art Unit 3792	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
TAMMIE K MARLEN	Primary Examiner	Telephonic
Kiri Lee Sharon	Attorney of Record	

Date of Interview: 30 August 2022

Issues Discussed:

Other

Applicant's representative inquired about why the "N2" document on the IDS of 8/15/2022 was lined-through. The Examiner indicated that there does not appear to be a patent number "5,211,938-B1" published on 07-08-1997 when searching for this document. Such a document is the Reexamination Certificate that is found at the end of U.S. Patent 5,211,938, so the reexamination certificate was considered as part of the consideration of U.S. Patent 5,211,938, but the entry was lined-through so as to not create confusion when the patent is printed.

/TAMMIE K MARLEN/ Primary Examiner, Art Unit 3792	
<p>Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04</p> <p>Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing</p>	

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.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor Name: Thomas BOYAJIAN

Title: ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY
AND DIAGNOSIS

Appl. No.: 16/791,004

Filing Date: 2/14/2020

Examiner: Tammie K. MARLEN

Art Unit: 3792

Conf. No.: 2631

**RESPONSE TO CORRECTED NOTICE OF ALLOWABILITY AND RECORD OF
INTERVIEW SUBSTANCE**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

Applicant thanks Primary Examiner Marlen for the issuance of the Corrected Notice of Allowability on August 24, 2022 in response to the Information Disclosure Statement (IDS) filed August 15, 2022. The PTO-issued interview summary mailed September 7, 2022 regarding the IDS is accurate.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741.

Respectfully submitted,

Date: 19 Sep 2022

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4092
Facsimile: (202) 672-5399

By /Kiri Lee Sharon/

Kiri Lee Sharon
Attorney for Applicant
Registration No. 71,828

Electronic Acknowledgement Receipt

EFS ID:	46644696
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Kiri Lee Sharon/Effie Hale
Filer Authorized By:	Kiri Lee Sharon
Attorney Docket Number:	067286-0410
Receipt Date:	19-SEP-2022
Filing Date:	14-FEB-2020
Time Stamp:	15:09:30
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant summary of interview with examiner	067286-0410_RecordInterview Substance.pdf	109483 0299d5716a17e8aab8e891f7368a49dba179e12b	no	1

Warnings:

Information:	
Total Files Size (in bytes):	109483
<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>	

**REQUEST FOR RECALCULATION OF PATENT TERM ADJUSTMENT
IN VIEW OF SAFE HARBOR STATEMENT UNDER 37 CFR 1.704(d)**

Application Number: 16/791,004	Patent Number: 11,446,512
Filing Date: 2/14/2020	Attorney Docket Number: 067286-0410
Applicant: DUSA PHARMACEUTICALS, INC.	
<p>Patentee hereby requests Recalculation of the Patent Term Adjustment (PTA) under 35 U.S.C. 154(b).</p> <p>A Request for Recalculation of PTA under this interim procedure is not considered a Request for Reconsideration within the meaning of 35 U.S.C. 154(b)(3) and 37 CFR 1.705(b). A Recalculation of Patent Term Adjustment under this interim procedure is not the Director's decision on patentee's request for reconsideration within the meaning of 35 U.S.C. 154(b)(3) and (b)(4).</p> <p>NOTE: This form may be used if the sole basis for requesting reconsideration of PTA is failure of the USPTO to recognize that an IDS was accompanied by a safe harbor statement under 37 CFR 1.704(d).</p>	
Signature /Kiri Lee Sharon/	Date 2 Nov 2022
Typed or printed name Kiri Lee Sharon	Practitioner Registration Number 71,828
<p>Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.</p>	
☒ *Total of <u>1</u> forms are submitted.	

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosures shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	46944130
Application Number:	16791004
International Application Number:	
Confirmation Number:	2631
Title of Invention:	ADJUSTABLE ILLUMINATOR FOR PHOTODYNAMIC THERAPY AND DIAGNOSIS
First Named Inventor/Applicant Name:	Thomas Boyajian
Customer Number:	22428
Filer:	Kiri Lee Sharon/Effie Hale
Filer Authorized By:	Kiri Lee Sharon
Attorney Docket Number:	067286-0410
Receipt Date:	02-NOV-2022
Filing Date:	14-FEB-2020
Time Stamp:	13:13:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request Recalculation Patent Term Adjustment(PTA) of Safe Harbor under 37 CFR 1.704(d)	067286-0410_ReqCalculationPTA_sb0134.pdf	884559 c4216b1918af4aa12abb6d46063b941808751cb9	no	2

Warnings:

Information:	
Total Files Size (in bytes):	884559
<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>	



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/791,004	02/14/2020	Thomas Boyajian	067286-0410	2631
22428	7590	03/15/2023		
FOLEY & LARDNER LLP 3000 K STREET N.W. SUITE 600 WASHINGTON, DC 20007-5109			EXAMINER MARLEN, TAMMIE K	
			ART UNIT	PAPER NUMBER
			3792	
			NOTIFICATION DATE	DELIVERY MODE
			03/15/2023	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):

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In re Application of	:	REDETERMINATION OF
DUSA Pharmaceuticals, Inc.	:	PATENT TERM ADJUSTMENT
Application No. 16/791,004	:	AND NOTICE OF INTENT
Filed: 14 Feb 2020	:	TO ISSUE
Patent No. 11,446,512	:	CERTIFICATE OF CORRECTION
Issued: 20 Sep 2022	:	
Docket No. 067286-0410	:	

This is a redetermination of the patent term adjustment in response to the “REQUEST FOR RECALCULATION OF PATENT TERM ADJUSTMENT IN VIEW OF SAFE HARBOR STATEMENT UNDER 37 CFR 1.704(d)”, filed November 2, 2022.

This redetermination of patent term adjustment is not the Director's decision on the applicant's request for reconsideration for purposes of seeking judicial review under 35 U.S.C. §154(b)(4).

On September 20, 2022, the instant application issued as Patent No. 11,446,512, with a patent term adjustment of 5 days. The Office determined a patent term adjustment of 5 days based upon 194 days of “A” delay, reduced by 189 days of Applicant delay. Patentee timely filed the instant request for recalculation within two months of the issue date.

Discussion

37 CFR 1.704(d)(1) states, in part:

A paper containing only an information disclosure statement in compliance with §§ 1.97 and 1.98 will not be considered a failure to engage in reasonable efforts to conclude prosecution (processing or examination) of the application under paragraphs (c)(6), (c)(8), (c)(9), or (c)(10) of this section if it is accompanied by a statement that each item of information contained in the information disclosure statement:

(i) 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; or

(ii) Is a communication that was issued by a patent office in a counterpart foreign or international application or by 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.

A review of the Information Disclosure Statement filed on August 15, 2022 reveals that it contained a 37 CFR 1.704(d) statement. In light of 37 CFR 1.704(d), no Applicant delay should have been assessed for this IDS (the Office had assessed 91 days of Applicant delay).

Overall PTA Calculation

Formula:

“A” delay + “B” delay + “C” delay - Overlap - applicant delay = X

USPTO’s Calculation:

194 + 0 + 0 – 0 – 98 = 96

Conclusion

The application is being forwarded to the Certificate of Corrections Branch for issuance of a certificate of correction. The Office will issue a certificate of correction indicating that the term of the above-identified patent is extended or adjusted by **ninety-six (96) days**.

Telephone inquiries specific to this matter should be directed to the undersigned at (571) 272-3207.

/Cliff Congo/

Cliff Congo
Attorney Advisor
Office of Petitions

Enc: draft Certificate of Correction

UNITED STATES PATENT AND TRADEMARK OFFICE
DRAFT CERTIFICATE OF CORRECTION

PATENT : 11,446,512

DATED : **September 20, 2022**

INVENTOR(S) : Boyajian et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the cover page,

[*] Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 USC 154(b) by 5 days.

Delete the phrase “by 5 days” and insert – by 96 days--