Electronic Acknowledgement Receipt

EFS ID:	24780389
Application Number:	15012532
International Application Number:	
Confirmation Number:	9345
Title of Invention:	EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF
First Named Inventor/Applicant Name:	Thomas B. Ottoboni
Customer Number:	108547
Filer:	Susan L. Harlocker/Julie Costello
Filer Authorized By:	Susan L. Harlocker
Attorney Docket Number:	092459-0173/8032
Receipt Date:	01-FEB-2016
Filing Date:	
Time Stamp:	17:52:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$1050
RAM confirmation Number	4966
Deposit Account	505907
Authorized User	HARLOCKER, SUSAN

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

Charge any Additional Fees required under 37 CFR 1.17 (Patent ap

Azurity Ex. 1039
PGR Petition – USP 12,115,255

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Charge any Additional Fees required under 37 CFR 1.17 (Patent application and reexamination processing fees)

Charge any Additional Fees required under 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	Drawings-only black and white line drawings	092459_0173_Fig1to4.pdf	988670 30b7681c1652efe92ccb308fa1f35143a3e5cfb5	no	4
Warnings:					
Information:					
2	Oath or Declaration filed	092459_0173_decs.pdf	950818 27f7176cb3f2978246a987a4e45836195520 4b7c	no	2
Warnings:					
Information:					
3	Application Data Sheet	092459_0173_ads.pdf	442056 730469ab831f5a2fafefca41532fd939e4ece b6f	no	7
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
4		092459_0173_appln.pdf	2964366 5affbbfa88e28cad275b8ca2b40a298ea19c 6428	yes	46

Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	42
Claims	43	45
Abstract	46	46

Warnings:	
Information:	
Total Files Size (in bytes):	5382982

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.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/012,532	02/01/2016	Thomas B. Ottoboni	092459-0173/8032	9345

108547 7590 11/04/2016
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER
HEYER, DENNIS

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
11/04/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mweipdocket@mwe.com

Office Action Summary	Application No. 15/012,532	Applicant(s) OTTOBONI ET AL.	
	Examiner DENNIS HEYER	Art Unit 1628	AIA (First Inventor to File) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 2 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 1-28.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) 1-28 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☐ Claim(s) _____ is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☒ Claim(s) 1-28 are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 – 17, drawn to an injectable emulsion comprising: a neurokinase-1 (NK-I) receptor antagonist; 11 wt/wt% to 15 wt/wt% of an emulsifier; an oil; a co-surfactant which comprises an alcohol; a tonicity agent; a pH modifier; and water; wherein the pH of the emulsion ranges from about 7.5 to 9.0; classified in class 546, subclass 82.

II. Claims 18 – 25, drawn to a method for preparing a pharmaceutical emulsion comprising: (a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase; (b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase; (c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and (d) sterilizing the pharmaceutical emulsion.

III. Claims 26 – 28, drawn to a method for treating a subject in need thereof, comprising administering to the subject a composition comprising the emulsion according to claim 1.

IV. Claims 26 – 28, drawn to a method for preventing a subject in need thereof, comprising administering to the subject a composition comprising the emulsion according to claim 1.

The inventions are distinct, each from the other because of the following reasons:

Inventions **I** and **III** (or **IV**)are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the product as claimed, a compound of formula (I), can be used in the materially different processes such as in vitro toxicity testing.

Inventions **II** and **I** are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product as claimed, an injectable emulsion

according to Claim 1, can be prepared by sterilizing each of the oil and aqueous phases prior to forming an emulsion.

Inventions **II** and **III** (or **IV**) are directed to related methods of making and methods of use. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed define different outcomes or effects by reciting distinct endpoints, specifically, making an injectable emulsion using the specific steps recited in Claim 18, as opposed to the method of administering an injectable emulsion to a subject to treat or prevent a condition. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and/or examination burden if restriction were not required because at least the following reason(s) apply:

The invention of Group II requires a search for specific emulsion forming steps not required by Groups I, III or IV. Finally the invention of Groups III or IV require search queries drawn to specific patient populations and specific conditions (nausea or vomiting), neither of which is required by Groups I or II.

Applicant is advised that the reply to this requirement to be complete <u>must</u> include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Species Elections

This application contains claims directed to the following patentably distinct species:

Applicant is required to elect:

a) A single injectable emulsion specie, said emulsion containing a single combination of each of a single claimed or otherwise disclosed neurokinase-1 (NK-I) receptor antagonist; emulsifier oil; a co-surfactant, alcohol, tonicity agent and pH modifier.

If Applicant elects Group III or IV, Applicant is FURTHER required to elect:

b) A single, condition from those recited in Claim 27 or otherwise disclosed.

If Applicant elects the condition of Claim 27, Applicant is FURTHER required to elect:

c) A form of inducing nausea/vomiting from those recited in Claim 28.

The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species, for example, species elections drawn to specific chemical compounds are defined by a unique set of physical and chemical properties and are prepared by a different method. Further, the disorder species are distinct because they are drawn to different patient populations. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect from specie (a) – (c), as defined above, to which the claims shall be restricted if no generic claim is finally held to be allowable. **The reply must also identify the claims readable on the elected species, including any claims subsequently added.**

There is an examination and search burden (e.g., searching different classes/subclasses or electronic resources, or employing different search queries) for

these patentably distinct compound species due to their mutually exclusive characteristics (structure, physical and chemical properties, etc.) which require different fields of search. Further, the patentably distinct disorder species are drawn to different patient populations and thus search queries for one disorder will not encompass the subject matter for all disorder species recited.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the

case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Multiple Inventors

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Notice of Possible Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 7AM-6PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, WINSTON SHEN can be reached at (571)272-3157. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Primary Examiner, Art Unit 1628

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Examiner: Heyer, Dennis
Ottoboni	Art Unit: 1628
Application No.: 15/012,532	Conf. No: 9345
Filed: February 1, 2016	
For: **EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF**	

RESPONSE TO REQUIREMENT FOR RESTRICTION AND/OR ELECTION

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

Commissioner:

The present communication is in response to the Restriction Requirement mailed November 4, 2016 in the above-identified application.

Amendments to the Claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

[The remainder of this page intentionally left blank.]

Amendments to the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1.**(Currently amended)** An injectable pharmaceutical emulsion comprising:

a neurokinase-1 (NK-1) receptor antagonist;

11 wt/wt% to 15 wt/wt% of an emulsifier;

an oil;

a co-surfactant which comprises an alcohol;

a tonicity agent;

a pH modifier; and

water;

wherein the pH of the emulsion ranges from about 7.5 to 9.0.

2. **(Original)** The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt%).

3. **(Original)** The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 10:1 to 15:1 (wt/wt%).

4. **(Original)** The emulsion according to claim 1, wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 10:1 to 30:1 (wt/wt%).

5. **(Original)** The emulsion according to claim 1, wherein the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 15:1 to 30:1 (wt/wt%).

6. **(Original)** The emulsion according to claim 1, wherein the ratio of emulsifier to oil ranges from about 1:1 to 3:1 (wt/wt%).

7. **(Original)** The emulsion according to claim 1, wherein the emulsifier is a phospholipid.

8. **(Original)** The emulsion according to claim 1, wherein the emulsifier is an egg lecithin.

9. **(Original)** The emulsion according to claim 1, further comprising dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

10. **(Original)** The emulsion according to claim 1, wherein the NK-1 receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, vestipitant, serlopitant, maropitant, casopitant, befetupitant, and orvepitant.

11. **(Original)** The emulsion according to claim 1, wherein the pH modifier is sodium oleate or a salt thereof.

12. **(Original)** The emulsion according to claim 1, wherein the pH modifier is a buffer.

13. **(Original)** The emulsion according to claim 12, wherein the buffer is Tris buffer.

14. **(Original)** The emulsion according to claim 1, wherein the oil is soybean oil.

15. **(Original)** The emulsion according to claim 1, wherein the alcohol is ethanol.

16. **(Original)** The emulsion according to claim 15, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

17. **(Original)** The emulsion according to claim 1, wherein the NK-1 receptor antagonist is not aprepitant.

18. **(Withdrawn, Currently amended)** A method for preparing a<u>n injectable</u> pharmaceutical emulsion comprising:

(a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase;

(b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase;

(c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and

(d) sterilizing the pharmaceutical emulsion.

19. **(Withdrawn)** The method according to claim 18, wherein step (c) comprises homogenizing the oil phase with the aqueous phase to generate a crude emulsion, and step (c) further comprises homogenizing the crude emulsion to generate a fine emulsion wherein the fine emulsion is the pharmaceutical emulsion.

20. **(Withdrawn)** The method according to claim 19, wherein homogenizing the crude emulsion comprises using a microfluidizer at a pressure between 10,000 to 30,000 psi.

21. **(Withdrawn)** The method according to claim 20, wherein homogenizing the crude emulsion comprises 4 to 15 passes through the microfluidizer.

22. **(Withdrawn)** The method according to claim 18, wherein the sterilizing comprising passing the pharmaceutical emulsion through a filter having a pore size of about 0.2 microns.

23. **(Withdrawn)** The method according to claim 18, further comprising adding a solution of dexamethasone sodium phosphate to the pharmaceutical emulsion prior to sterile filtration.

24. **(Withdrawn)** The method according to claim 18, wherein the receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, casopitant, befetupitant, vestipitant, serlopitant, maropitant, and orvepitant.

25. **(Withdrawn)** The method according to claim 18, wherein the NK-1 receptor antagonist is not aprepitant.

26. **(Withdrawn)** A method for preventing or treating a subject in need thereof, comprising administering to the subject a composition comprising the emulsion according to claim 1.

27. **(Withdrawn)** The method according to claim 26, wherein the subject is at risk of or is suffering from nausea and/or vomiting.

28. **(Withdrawn)** The method according to claim 27, wherein the nausea and/or vomiting is induced by chemotherapy, surgery, or radiotherapy.

REMARKS

Consideration of the remarks and amendments presented herein is respectfully requested.

I. Status of the Claims

Claims 1-28 are pending.

Claims 18-28 are withdrawn. Applicants reserve the right to pursue the withdrawn subject matter in a continuing application.

Applicants reserve the right to pursue at a later date in one or more continuing applications subject matter supported by the present disclosure, including subject matter which may be considered to be disclaimed herein.

I. Amendments to the Claims

Claims 1 and 18 are amended for clarity.

No new matter is added by way of these amendments.

II. Restriction Requirement

The Examiner required restriction to one of the following groupings of claims as set forth in the instant Office action to commence prosecution on the merits:

Group I: Claims 1-17 drawn to an injectable emulsion.

Group II: Claims 18-25 drawn to a method for preparing a pharmaceutical emulsion.

Group III: Claims 26-28 drawn to a method for treating a subject in need thereof.

Group IV: Claims 26-28, drawn to method for preventing a subject in need thereof,

In response, Applicants elect Group I, claims 1-17, without traverse. It is Applicants' understanding that claims 1-17 encompass the elected invention.

III. Conclusion

No fees are believed to be due with this response. The Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-5907.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to contact the undersigned at (650) 815-7647.

Respectfully submitted,
McDermott Will & Emery LLP

Date: December 30, 2016

/Susan L. Harlocker /
Susan L. Harlocker
Registration No. 59,144

Correspondence Address
Customer No. 108547

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/012,532	02/01/2016	Thomas B. Ottoboni	092459-0173/8032	9345

108547 7590 04/06/2017
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER
HEYER, DENNIS

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
04/06/2017	ELECTRONIC

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mweipdocket@mwe.com

Office Action Summary	Application No. 15/012,532	Applicant(s) OTTOBONI ET AL.	
	Examiner DENNIS HEYER	Art Unit 1628	AIA (First Inventor to File) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
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Status

1)☒ Responsive to communication(s) filed on *12/30/2016 and 1/29/2017*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1-28* is/are pending in the application.

5a) Of the above claim(s) *10,12,13 and 17-28* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-9,11 and 14-16* is/are rejected.

8)☒ Claim(s) *11* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date *4/25/2016 and 7/1/2016*.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Status of Claims

Claims 1 – 28 are currently pending.

Election/Restrictions

Applicant's election, without traverse, of Group I (Claims 1 – 17) in the response filed on December 30, 2016 is acknowledged. Claims 18 – 28, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim.

Acknowledgement is made of Applicant's election, in a voice mail message left by Susan L. Harlocker on January 29, 2017, of a single injectable emulsion specie, said emulsion comprising:

a) 'aprepitant' as the neurokinase-1 (NK-1) receptor antagonist

b) 'egg lecithin' as the emulsifier

c) 'soybean oil' as the oil

d) 'ethanol' as the alcohol co-surfactant

e) 'sucrose' as the tonicity agent, and

f) 'sodium oleate' as the pH modifier

Claims 12 and 13 (requiring a Tris buffer), and Claims 10 and 17 (which exclude aprepitant) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as

being drawn to a nonelected injectable emulsion specie, there being no allowable generic or linking claim. It is noted that, as disclosed on p [0019] of the specification, the pH modifier sodium oleate is distinct from a 'buffer'.

Claims 10, 12, 13 and 17 – 28 are withdrawn. Claims 1 – 9, 11 and 14 – 16 are under examination in the instant office action.

Priority

This application, 15/132,130, was filed 02/01/2016.

Claim Objections

Claim 11 is objected to over the language “sodium oleate or a salt thereof”. Sodium oleate is already a salt, thus a salt of the salt sodium oleate is confusing.

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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.

Claims 1 – 8 and 14 – 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 (published: March 21, 2012; IDS dated 4/25/2016; Foreign Patent Document Cite No. 1, English Translation provided) in view of Booth *et al.* in US 2013/0236501 (published: September 12, 2013; IDS dated 4/25/2016, US Patent Document Cite No. 3).

Zhou teaches an injectable microemulsion composition comprising the neurokinin-1 (NK-1) receptor antagonist aprepitant (Claim 1). Zhou teaches aprepitant is used orally in capsules to treat vomiting (emesis) induced by cancer chemotherapy but that oral administration is very inconvenient to patients. Zhou teaches that aprepitant injectable microemulsions can overcome the disadvantage of oral aprepitant formulations (poor absorption, low bioavailability etc.) (p [0006] – [0007]).

Zhou teaches, in Claim 9:

9. The aprepitant microemulsion for injection according to claim 1, characterized in that it is consisting of the following components in percentages by mass: 1.0% - 1.5% of aprepitant, 7% - 15% of oil for injection, 8% - 10% of emulsifier, 2% - 5% of co-emulsifier, 8% - 13% of protective agent, and 60% - 69% of water for injection.

Zhou teaches the oil is preferably the elected oil, soybean oil (instant Claims 1 and 14); the emulsifier is preferably the elected emulsifier, egg yolk phospholipid (i.e.

egg lecithin; instant Claims 1, 7 and 8); the co-emulsifier is preferably the elected alcohol, ethanol (instant Claims 1, 5 and 16) and the protective agent, preferably glycerin, may also be sucrose (the elected, as defined by Applicant, tonicity agent (instant Claim 1) (p [0010])

The ratio of the oil to compound 1 to the NK-1 receptor antagonist aprepitant ranges from 15:1 to 4.67:1 wt/wt% which encompasses and thus renders *prima facie* obvious the ranges recited in instant Claims 2 and 3. The ratio of emulsifier to the NK-1 receptor antagonist aprepitant ranges from 10:1 to 5.33:1 wt/wt% which overlaps with and thus renders *prima facie* obvious the ranges recited in instant Claims 4 and 5. The ratio of emulsifier to oil ranges from 1.43:1 to 0.53:1 wt/wt% which overlaps with and thus renders *prima facie* obvious the ranges recited in instant Claim 6. See MPEP 2144.05: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Zhou teaches "adjusting [modifying] the pH to 6.0 – 8.0 to obtain a primary emulsion" (Claim 10), which renders the addition of a pH modifier (instant Claim 1) implicit in the emulsion composition.

Zhou teaches several specific emulsion preparations such as, in Example 7 (p [0031] – [0032]), a 100 g microemulsion for injection consisting of the following components, wherein each weight represents a 'weight percent': 0.2 g aprepitant (the elected NK-1 antagonist), 9.5 g soybean oil (the elected oil; instant Claims 1 and 14), 9.8 g egg yolk phospholipid (i.e. lecithin, the elected emulsifier; instant Claims 1, 7 and

8), 5.5 g ethanol (the elected alcohol; instant Claims 1, 15 and 16), 1 g glycerin (a protective agent, Claim 1; or, a 'tonicity agent'; as evidenced by p [0106] of the present specification; instant Claim 1) and 74 g water (instant Claim 1). Zhou teaches the oil and aqueous phases were mixed and the pH adjusted (reasonably construed as requiring the addition of a pH modifier) to 8.0 (p [0033]; instant Claim 1).

The amount of emulsifier (8 – 10 wt. %, with a specific example, Example 5, containing 10 wt.% egg yolk phospholipid) in the aprepitant emulsion compositions of Zhou is slightly lower than the range recited in instant Claim 1 (11 – 15% wt/wt%).

However, as discussed in MPEP 2144.05(I) "a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)." In the present case it would have been *prima facie* obvious to modify the elected emulsifier, egg yolk lecithin, in an almost identical prior art injectable aprepitant emulsion composition, from 10 wt% to 11 wt% because there would have been a reasonable expectation that said modification would have resulted in an emulsion composition having essentially the same properties, absent specific evidence to the contrary.

Alternatively, Booth teaches injectable oil-in-water emulsions of sedative hypnotic agents (Title, Abstract). Booth teaches the emulsions comprise a substituted phenylacetic acid ester compound; a water-immiscible solvent (including soybean oil, p [0037]); an emulsifier (lecithin, Claim 13); a tonicity modifier (glycerol, Claim 17); and

water; and optionally further comprising one or more of the following selected from a pH buffering agent, a stabilizer (oleic acid, Claim 26), and an additive; wherein the pH of the emulsion is greater than about 7 (Claim 1)

Booth teaches both egg (Lipoid E80) and soy (Lipoid S75)-derived lecithin are used as emulsifiers (p [0092], Table) and an embodiment wherein the amount of emulsifier in the emulsions varies from about 0.001 wt % to about 15 wt % (p [0041]). The amount of emulsifier in the emulsions of Booth encompass or overlap those recited in instant Claim 1. See MPEP 2144.05: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to modify the injectable emulsion compositions of Zhou with an amount of lecithin emulsifier ranging from 8 wt.% to 15 wt%. One would have been motivated to do so, with a reasonable and predictable expectation of success because Zhou and Booth teach injectable oil-in-water emulsion compositions containing the similar components (soybean oil, lecithin, oleic acid/oleate glycerin/glycerol) and pH range wherein the amount of lecithin emulsifier can vary from 8 wt% to 15 wt%.

Moreover, as discussed in MPEP 2144.05 (II), it has been held that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Applicants have not demonstrated any unexpected or unusual results, which accrue from the instantly claimed wt% range of emulsifier. In the present case Applicant appears to have merely optimized the % wt. of emulsifier (a component art-recognized to aid in the formation of emulsions) using amounts that fall within ranges taught in the prior art (8 wt% to 15 wt%), by routine experimentation, to arrive at the claimed injectable emulsion composition. See also, in MPEP 2144.05 (II): Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

Moreover, it is noted that because emulsifiers are known to aid in the formation of emulsions, varying their amounts equates to a result-effective variable, i.e., a variable which achieves a recognized result, and thus the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)

It is noted that Applicants can rebut a prima facie case of obviousness based on overlapping ranges by showing the criticality of the claimed range. "The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims. . . . In such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range." In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). See MPEP § 716.02 - § 716.02(g) for a discussion of criticality and unexpected results.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 (published: March 21, 2012) in view of Booth *et al.* in US 2013/0236501 (published: September 12, 2013), as applied to the rejection of Claims 1 – 8 and 14 – 16 in the 103(a) rejection above, and further in view of Wan *et al.* in US2011/0038925 (published: February 17, 2011).

As discussed in the 103(a) rejection above, Zhou in combination with Booth render obvious the injectable emulsion composition of Claims 1 – 8 and 14 – 16 comprising the NK-1 antagonist aprepitant for the treatment of nausea and/or emesis.

Zhou in combination with Booth do not render obvious an injectable emulsion further comprising sodium oleate (the Applicant-defined pH modifier).

Wan teaches Pharmaceutical compositions for intravenous administration (i.e. the formulations are injectable) comprising a Neorokinin-1 (NK-1) antagonist compound of Formula I wherein said compositions are for treating nausea and/or emesis (Title. Abstract).

Wan teaches the compositions comprise a compound of Formula I and a vehicle selected from the group consisting of water soluble organic solvents, non-ionic surfactants, water insoluble lipids, organic lipids/semisolids and phospholipids and wherein the water soluble organic solvents include ethanol, the water insoluble lipids include soybean oil, the organic liquids and semisolids include oleic acid and the phospholipids include lecithin. Wan teaches an embodiment wherein the composition is in the form of a microemulsion and having a pH from about 6.5 to 8.0 (p [0057] – [0058]).

Wan teaches compositions wherein lecithin is the preferred emulsifier, and purified egg lecithin (the elected emulsifier) is the most preferred. Wan teaches oleic acid or sodium oleate (Applicant-defined and elected pH modifier) as an added stabilizer, and that medium chain (Myglyol) and long chain (Soybean oil; the elected oil) triglycerides may also be added. Added emulsifiers include egg phosphatidyl choline as well as Lipoid E 80 or Lipoid E80S. Wan teaches glycerin may be used as a tonicity adjustor (i.e. a tonicity agent) and ethanol (the elected alcohol) may be used as a co-solvent/solubilizer for the lecithin and drug (compound of formula 1) (p [0338]).

Wan teaches, the composition in Example 15 (below):

TABLE 15

Materials	Composition %	Function
Compound 1*	0.4-1.5%	Drug/active
Egg PC	3.0%	Emulsifier
Lipoid E 80S	1.2%	Emulsifier
Lipoid E80	1.2%	Emulsifier
Sodium oleate	0.3%	Emulsifier
Glycerin	2.25%	Stabilizer/co-emulsifier
Ethanol	1.6-4.0%	Cosolvent
Myglyol (MCT)	5-10%	Solubilizer/hydrophobic component
Soybean Oil (LCT)	5-10%	Solubilizer/hydrophobic component

*compound 1 in the form of solid monohydrate hydrochloride salt
MCT = medium chain triglyceride;
LCT = long chain triglyceride/fatty acid

which contains the elected pH modifier sodium oleate (instant Claims 1 and 11).

It would have been *prima facie* obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to modify the injectable emulsion composition of Zhou and Booth with an amount of sodium oleate. One would have been motivated to do so, with a reasonable and predictable expectation of success because Wan teaches sodium oleate is advantageously added as a stabilizer/emulsifier

to injectable oil-in-water emulsion compositions containing similar components (NK-1 antagonist, soybean oil, lecithin, glycerin/glycerol) and pH range.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 (published: March 21, 2012) in view of Booth *et al.* in US 2013/0236501 (published: September 12, 2013), as applied to the rejection of Claims 1 – 8 and 14 – 16 in the 103(a) rejection above, and further in view of Cassileth *et al.* in Arch. Intern Med. 1983;143(7):1347 – 1349 (Abstract) and Dexamethasone Hydrogen Phosphate at web.archive.org/web/20141224130045/ http://www.drugs.com/pro/dexamethasone-sodium-phosphate.html.

As discussed in the 103(a) rejection above, Zhou in combination with Booth render obvious the injectable emulsion composition of Claims 1 – 8 and 14 – 16 comprising the NK-1 antagonist aprepitant for the treatment of nausea and/or emesis.

Zhou in combination with Booth do not teach an injectable emulsion formulation further comprising dexamethasone sodium phosphate.

Cassileth teaches the antiemetic efficacy of dexamethasone therapy in patients receiving cancer chemotherapy (Title). Cassileth teaches dexamethasone sodium phosphate (a phosphate salt of dexamethasone) when administered intravenously before therapy resulted in no GI intolerance in 83% of patients compared to 57% in placebo trials (Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art, before the effective filing date of the claimed invention, to modify the injectable emulsion compositions of Wan and Booth with an amount of dexamethasone sodium phosphate.

One would have been motivated to do so, with a reasonable and predictable expectation of success because the prior art teaches that aprepitant (Zhou and Booth) and dexamethasone sodium phosphate (Cassileth) are known to be effective for the treatment of nausea and/or emesis. As discussed in MPEP 2144.06: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

The combination of Zhou, Booth and Cassileth do not explicitly teach that the dexamethasone sodium phosphate of Cassileth, when formulated with the emulsion of Zhou and Booth, would be present in the aqueous phase. However, as discussed in web.archive.org/web/20141224130045/http://www.drugs.com/pro/dexamethasone-sodium-phosphate.html, dexamethasone sodium phosphate is freely soluble in water. Accordingly, it would have flowed naturally during the step of forming the emulsion of Zhou and Booth, that the freely water soluble dexamethasone sodium phosphate would be present in the aqueous phase of the formed emulsion, absent specific evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit http://www.uspto.gov/forms/. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more

information about eTerminal Disclaimers, refer to

http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1 – 9, 11 and 14 – 16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 – 11 of US patent 9,561,229.

Although the copending and instant claims are not identical, they are not patentably distinct from each other because the instant and patented claims each recite an injectable pharmaceutical emulsion comprising aprepitant, egg yolk lecithin, soybean oil, sodium oleate, ethanol and a tonicity agent (sucrose) in a pH that ranges from 7.5 to 9.0, and in amounts that that at least overlap with, and thus render *prima facie* obvious, the instant and patented claims.

Claims 1 – 9, 11 and 14 – 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 18 and 20 – 34 of copending US patent application serial No. 14/859,013.

Although the copending (method of treating) and instant claims (product) are not identical, they are not patentably distinct from each other because the instant and copending claims each recite the same injectable pharmaceutical emulsion comprising aprepitant, egg yolk lecithin, soybean oil, sodium oleate, ethanol and a tonicity agent (sucrose) in a pH that ranges from 7.5 to 9.0.

Conclusion

Claims 1 – 9, 11 and 14 – 16 are rejected. Claim 11 is objected to. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 7AM-6PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, WINSTON SHEN can be reached at (571)272-3157. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Primary Examiner, Art Unit 1628

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Examiner: Heyer, Dennis
Ottoboni and Han	Art Unit: 1628
Application No.: 15/012,532	Conf. No: 9345
Filed: February 1, 2016	
For: **EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF**	

RESPONSE UNDER 37 C.F.R. § 1.111

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

Commissioner:

The present communication is in response to the non-final Office Action mailed April 6, 2017, in the above-identified application. A two-month extension of time is concurrently requested.

Amendments to the Claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

[The remainder of this page intentionally left blank.]

Amendments to the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1.(Currently Amended) An injectable pharmaceutical emulsion comprising:

a neurokinase-1 (NK-1) receptor antagonist;

11 wt/wt% to 15 wt/wt% of an emulsifier;

an oil;

a co-surfactant which comprises an alcohol;

a tonicity agent;

a pH modifier; and

water;

wherein the pH of the emulsion ranges from about 7.5 to 9.0, and the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt%).

2. (Original) The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt%).

3. (Original) The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 10:1 to 15:1 (wt/wt%).

4. (Cancelled)

5. (Cancelled)

6. (Original) The emulsion according to claim 1, wherein the ratio of emulsifier to oil ranges from about 1:1 to 3:1 (wt/wt%).

7. (Original) The emulsion according to claim 1, wherein the emulsifier is a phospholipid.

8. (Original) The emulsion according to claim 1, wherein the emulsifier is an egg lecithin.

9. (Original) The emulsion according to claim 1, further comprising dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

10. (Original) The emulsion according to claim 1, wherein the NK-1 receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, vestipitant, serlopitant, maropitant, casopitant, befetupitant, and orvepitant.

11. (Original) The emulsion according to claim 1, wherein the pH modifier is an ~~sodium~~ oleate or a salt thereof.

12. (Original) The emulsion according to claim 1, wherein the pH modifier is a buffer.

13. (Original) The emulsion according to claim 12, wherein the buffer is Tris buffer.

14. (Original) The emulsion according to claim 1, wherein the oil is soybean oil.

15. (Original) The emulsion according to claim 1, wherein the alcohol is ethanol.

16. (Original) The emulsion according to claim 15, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

17. (Original) The emulsion according to claim 1, wherein the NK-1 receptor antagonist is not aprepitant.

18. (Withdrawn, Previously Presented) A method for preparing an injectable pharmaceutical emulsion comprising:

(a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase;

(b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase;

(c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and

(d) sterilizing the pharmaceutical emulsion.

19. (Withdrawn) The method according to claim 18, wherein step (c) comprises homogenizing the oil phase with the aqueous phase to generate a crude emulsion, and step (c) further comprises homogenizing the crude emulsion to generate a fine emulsion wherein the fine emulsion is the pharmaceutical emulsion.

20. (Withdrawn) The method according to claim 19, wherein homogenizing the crude emulsion comprises using a microfluidizer at a pressure between 10,000 to 30,000 psi.

21. (Withdrawn) The method according to claim 20, wherein homogenizing the crude emulsion comprises 4 to 15 passes through the microfluidizer.

22. (Withdrawn) The method according to claim 18, wherein the sterilizing comprising passing the pharmaceutical emulsion through a filter having a pore size of about 0.2 microns.

23. (Withdrawn) The method according to claim 18, further comprising adding a solution of dexamethasone sodium phosphate to the pharmaceutical emulsion prior to sterile filtration.

24. (Withdrawn) The method according to claim 18, wherein the receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, casopitant, befetupitant, vestipitant, serlopitant, maropitant, and orvepitant.

25. (Withdrawn) The method according to claim 18, wherein the NK-1 receptor antagonist is not aprepitant.

26. (Withdrawn) A method for preventing or treating a subject in need thereof, comprising administering to the subject a composition comprising the emulsion according to claim 1.

27. (Withdrawn) The method according to claim 26, wherein the subject is at risk of or is suffering from nausea and/or vomiting.

28. (Withdrawn) The method according to claim 27, wherein the nausea and/or vomiting is induced by chemotherapy, surgery, or radiotherapy.

REMARKS

Consideration of the remarks and amendments presented herein is respectfully requested.

I. Status of the Claims

Without prejudice or disclaimer, claims 4 and 5 are cancelled.

Claim 1 is amended to indicate that the weight percentage ratio of the emulsifier to the NK-1 receptor antagonist ranges from 18:1 to 22:1, support for which can be found in the specification as filed, for example, at ¶ [0029]. Claim 11 is amended herein to more clearly reflect the nature of the claimed subject matter. There is no issue of new matter.

Applicants reserve the right to pursue at a later date in one or more continuing applications subject matter supported by the present disclosure, including subject matter which may be considered to be disclaimed herein.

Upon entry of this paper, claims 1-3 and 6-17 are pending and under examination. Claims 18-28 are withdrawn. Applicants reserve the right to pursue the withdrawn subject matter in a continuing application.

II. Claim Objection

Claim 11 is objected to over the language "sodium oleate or a salt thereof" because oleate is already a salt. Applicant has amended claim 11 to change "sodium oleate" into "an oleate." This objection should be withdrawn.

III. Claim Rejections – 35 U.S.C. § 103

Claims 1-8 and 14-16 are rejected under 35 U.S.C. § 103(a) over CN102379845 ("Zhou") in view of Booth et al. in US 2013/0236501 ("Booth"). Office Action at pp. 4-9.

Claim 11 is rejected under 35 U.S.C. §103(a) over Zhou in view of Booth, as applied to the rejection of claims 1-8 and 14-16 above, and further in view of US 2011/0038925 ("Wan"). Id.at pp. 9-11.

Claim 9 is rejected under 35 U.S.C. §103(a) over Zhou in view of Booth as applied to the rejection of claims 1-8 and 14-16 above, and further in view of Arch. Intern. Med., 1983, 143(7): 1347-1349 (Abstract) by Cassileth et al. ("Cassileth") and Dexamethasone Hydrogen

Phosphate at web.archive.org/20141224130045/http://www.drugs.com/pro/dexamethasone-sodium-phosphate.html ("Web Archive").

The above rejections are respectfully traversed for the reasons below.

In making the rejections, the Office cites Zhou for teaching an injectable microemulsion composition comprising NK-1 receptor antagonist aprepitant (1.0-1.5 wt%), oil for injection (7-15 wt%), emulsifier (8-10 wt%), co-emulsifier (2-5 wt%), protective agent (8-13 wt%), and water (60-69%). Office Action at p.4. According to the Office, Zhou further teaches that the oil, emulsifier, co-emulsifier, and the protective agent can be the corresponding elected species, such as soybean oil as the elected oil, egg yolk phospholipid as the elected emulsifier, ethanol as the elected co-emulsifier, and sucrose as the elected tonicity agent. Id. at pp.4-5. The Office further considers addition of a pH modifier as being implicitly taught by Zhou because of Zhou's disclosure "adjusting [modifying] the pH to 6.0-8.0 to obtain a primary emulsion." Id. at p. 5.

The Office admits that the range of emulsifiers (8-10 wt%) taught by Zhou is outside the instantly claimed range of 11-15 wt% for the emulsifier. Id. at p. 6. The Office contends that absent specific evidence to the contrary, it would have been obvious to modify the elected emulsifier from 10 wt to 11 wt because there would be a reasonable expectation that said modification would have resulted in an emulsion composition having essentially the same properties. Id. Alternatively, the Office argues that a skilled artisan would modify the injectable emulsion compositions of Zhou with an amount of lecithin emulsifier ranging from 8 % to 15 wt% in view of Booth's disclosure of an injectable oil-in water emulsions of sedative hypnotic agents comprising, in one embodiment for example, emulsifier in the amount from about 0.001 to 15 wt%. Applicant respectfully disagrees.

The References Fail to Teach Each and Every Element of Claim 1, as Amended

Claim 1, as amended, recites, in relevant part, that the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt%). Booth has nothing to do with NK-1 receptor antagonist. Zhou discloses optimized weight percentages for aprepitant and the emulsifier as 1.0-1.5 wt% and 8-10 wt%, respectively. Zhou, ¶[0009]. Zhou does not teach or suggest the weight percentage ratio of aprepitant to the emulsifier. If anything concerning the ratio can be inferred from Zhou's disclosure from mathematics point of view, Zhou may disclose an optimized weight percentage ratio of aprepitant to the emulsifier ranges from 5.4:1

(8%/1.5%) to 10:1 (10%/1.0%), which, however, is significantly outside the currently claimed range of 18:1 to 22:1.

To be sure, Zhou also broadly discloses that the weight percentage for aprepitant can be 0.05-2% and for the emulsifier can be 0.5-10%. Again, that does not constitute a disclosure of the weight percentage ratio of aprepitant to the emulsifier. From mathematics point of view, Zhou may be said to disclose a weight percentage ratio of aprepitant to the emulsifier ranges from 0.25:1 (0.5%/2%) to 200:1 (10%/0.05%). This broad range by itself, however, does not render the currently claimed range of 18:1 to 22:1 obvious. See MPEP § 2144.05 (I).

No Motivation to Combine the References in a Manner to Arrive at the Instant Claims

"The rationale to support a conclusion that the claim would have been obvious is that 'a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so.'" MPEP §2143. Here, neither Zhou nor Booth would motivate one of ordinary skill in the art to modify the weight percentage of the emulsifier into the currently claimed range. Zhou teaches that the weight percentage of 8-10% for the emulsifier is the optimized percentage. Zhou, ¶ [0009]. Booth teaches an emulsion which has nothing to do with NK-1 receptor antagonist. Moreover, when discussing the amount of the emulsifier, Booth states at ¶[0041]:

> The amount of emulsifier used in the emulsions of the present invention may vary from about 0.001 wt % to about 15 wt %. In one embodiment, the amount ranges from about 0.01 wt % to about 10 wt %. In another embodiment, the amount ranges from about 0.01 wt % to about 5 wt %. In a further embodiment, the amount ranges from about 0.1 wt % to about 2.5 wt %.

That is to say, Booth teaches the amount of the emulsifier to be trending away from the higher end of its broadest range and directs one of ordinary skill in the art to an amount not more than 10 wt%. In other words, the Office has not established on the records as to why one of ordinary skill in the art would go against 1) Zhou's teaching of the optimized amount of 8-10 wt% for the emulsifier, and/or 2) Booth's direction to an amount of not more than 10 wt% for the emulsifier and change the amount of the emulsifier to be in the range of 11 wt% to 15 wt% so as to arrive at the instant claims.

Identification of the Source of a Problem Renders the Instant Claims Non-Obvious

Moreover, "[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under **35 U.S.C. § 103**." *In re Sponnoble,* 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969). MPEP § 2141.02(III).

The instant claims represent identification of a problem not previously recognized by Zhou or Booth and the remedy thereof[1]. In Example 4 of the instant specification as filed, an emulsion comprising less than 11 wt/wt% egg yolk lecithin (9.95 wt/wt% Lipoid E 80), which therefore is outside the scope of the instant claims, resulted in an emulsion in which crystals were observed within 4 days post preparation at room temperature. In the Declaration submitted September 1, 2016, in Application No. 15/083,071 (now US Patent No. 9,561,229)("Ottoboni Declaration"), Dr. Ottoboni confirmed that Example 4 of the instant application describes an emulsion that was prepared according to the methods taught by Zhou.

In contrast, as shown in Table 7 on pages 31-32 of the instant specification as filed, the formulations of Examples 1, 2, 3 and 6 with increased amount of the emulsifier were stable as demonstrated by the lack of crystal formation when the emulsions were stored at room temperature for at least 2 months in the case of Examples 1, 3 and 6, and for at least 3 months for Example 2. The pharmaceutical emulsions described in Examples 1, 2, 3 and 6, comprising Lipoid E 80 as the emulsifier in the amount of 13.6 wt%, 14.3 wt%, 11.7 wt%, and 13.8%, respectively, each falls within the scope of instant claim 1.

Neither Zhou nor Booth recognizes the formation of crystals in the emulsions produced as described in each of their references or the effects of 13 to 15 weight percent emulsifier on stability of an emulsion.

The Results are Unpredictable

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of

[1] In the Office Action, the Office also contends that there would have been a reasonable expectation that modification of the amount of the emulsifier would have resulted in an emulsion composition having essentially the same properties, absent specific evidence to the contrary. The evidence provided hereafter indeed shows that the amount of the emulsifier in the claimed range increase the stability of an emulsion, which is unexpected.

ordinary skill in the art. *KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. 538, 417, 82 USPQ2d 1385, 1396 (2007)" MPEP § 2143.01(III). Assuming that one of ordinary skill in the art would be motivated to modify the amount of the emulsifier to be within the range as recited in claim 1, the results are unpredictable with respect to, for example, the stability. As discussed above, the stability of an emulsion comprising an emulsifier in the the amount in accordance with the current claims is much improved compared to prior art emulsions comprising the emulsifier in an amount outside the scope of the current claims. The improved stability cannot be predicted. See the Ottoboni Declaration, ¶9.

For the foregoing reasons, claim 1 is non-obvious over Zhou and Booth. The Office has not shown that other cited references rectify the deficiencies of Zhou and Booth. Accordingly, claim 1 as well as claims 2-17 which depend from claim 1 are non-obvious. Applicant therefore respectfully request withdrawal of the section 103 rejections.

IV. Double Patenting

Claims 1-9, 11, and 14-16 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-11 of US Patent No.9,561,229. Office Action at p. 14.

Claims 1-9, 11, and 14-16 are provisionally rejected on the ground of non-statutory obviousness-type double patenting over claims 18 and 20-34 of co-pending Application No. 14/859,013.

Applicant hereby submits a terminal disclaimer to render moot these double patenting rejections.

V. Conclusion

The Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-5907.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to contact the undersigned at (650) 815-7399.

Respectfully submitted,
McDermott Will & Emery LLP

Date: September 6, 2017

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/012,532	02/01/2016	Thomas B. Ottoboni	092459-0173/8032	9345

108547 7590 12/01/2017
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER
HEYER, DENNIS

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
12/01/2017	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):

mweipdocket@mwe.com

Office Action Summary	Application No. 15/012,532	Applicant(s) Ottoboni et al.	
	Examiner DENNIS HEYER	Art Unit 1628	AIA Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 9/6/2017 .

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____ .

2a)☑ This action is **FINAL.** 2b) ☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☑ Claim(s) 1-3 and 6-28 is/are pending in the application.

5a) Of the above claim(s) 10,12-13 and 17-28 is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☑ Claim(s) 1-3,6-9,11 and 14-16 is/are rejected.

8)☑ Claim(s) 11 is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date 9/6/2017 .

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____ .

4) ☐ Other: _____ .

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

DETAILED ACTION

Acknowledgement is made of Applicant's remarks and amendments in the response filed September 6, 2017. Acknowledgement is made of Applicant's amendment to Claim 1 further limiting the scope of the ratio of the emulsifier to the NK-1 receptor antagonist, and the cancellation of Claims 4 and 5. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 1 – 3 and 6 – 28 are currently pending. Claims 10, 12, 13 and 17 – 28 are withdrawn. Claims 1 – 3, 6 – 9, 11 and 14 – 16 are under examination in the instant office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on September 6, 2017 was filed after the mailing date of the non-Final Office Action on April 6, 2017. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Withdrawn Rejections

Claim rejections – 35 USC § 103

The rejection of Claims 1 – 8 and 14 – 16 under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 in view of Booth *et al.* in US 2013/0236501 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1 limiting the scope of the injectable pharmaceutical emulsion to those having a ratio of emulsifier to the NK-1 receptor antagonist ranging from 18:1 to 22:1 (wt/wt%).

The rejection of Claim 11 under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 in view of Booth *et al.* in US 2013/0236501, and further in view of Wan *et al.* in US2011/0038925 is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1 limiting the scope of the injectable pharmaceutical emulsion to those having a ratio of emulsifier to the NK-1 receptor antagonist ranging from 18:1 to 22:1 (wt/wt%).

The rejection of Claim 9 under 35 U.S.C. 103(a) as being unpatentable over Zhou *et al.* in CN 102379845 in view of Booth *et al.* in US 2013/0236501, and further in view of Cassileth *et al.* in Arch. Intern Med. 1983;143(7):1347 – 1349 (Abstract) and Dexamethasone Hydrogen Phosphate at web.archive.org/web/20141224130045/http://www.drugs.com/pro/dexamethasone-sodium-phosphate.html, is rendered moot and is withdrawn in response to Applicant's amendment to Claim 1 limiting the scope of the

injectable pharmaceutical emulsion to those having a ratio of emulsifier to the NK-1 receptor antagonist ranging from 18:1 to 22:1 (wt/wt%).

Maintained Objections and Rejections

Claim Objections

Amended Claim 11 remains objected to, now over the language "an oleate or a salt thereof". An oleate is already a salt, thus a salt of an oleate is confusing. It appears that Applicant intended to recite language encompassing the genus of those compounds that are "salts of oleic acid".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*,

686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit http://www.uspto.gov/forms/. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1 – 9, 11 and 14 – 16 *remain* rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 – 11 of US patent 9,561,229.

Although the copending and instant claims are not identical, they are not patentably distinct from each other because the instant and patented claims each recite an injectable pharmaceutical emulsion comprising aprepitant, egg yolk lecithin, soybean oil, sodium oleate, ethanol and a tonicity agent (sucrose) in a pH that ranges from 7.5 to

9.0, and in amounts that that at least overlap with, and thus render *prima facie* obvious, the instant and patented claims.

Claims 1 – 9, 11 and 14 – 16 *remain* rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 – 15 of US patent 9,808,465. *It is noted that this ground of rejection is no longer provisional because copending US patent application serial No. 14/859,013 issued as US patent 9,808,465 on October 18, 2017.*

Although the copending (method of treating) and instant claims (product) are not identical, they are not patentably distinct from each other because the instant and copending claims each recite the same injectable pharmaceutical emulsion comprising aprepitant, egg yolk lecithin, soybean oil, sodium oleate, ethanol and a tonicity agent (sucrose) in a pH that ranges from 7.5 to 9.0.

Response to Arguments

Applicant states (Remarks, page 9):

> Applicant hereby submits a terminal disclaimer to render moot these double patenting rejections.

In response, it is noted that, contrary to Applicant's statement, no terminal disclaimers have been submitted. As such, because Applicant has not otherwise traversed the basis for the double patenting rejections, these rejections are maintained for reasons of record.

Conclusion

Claims 1 – 3, 6 – 9, 11 and 14 – 16 are rejected. Claim 11 is objected to. No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on 7-7 EST Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, WINSTON SHEN can be reached at (571)272-3157. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Primary Examiner, Art Unit 1628

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Examiner: Heyer, Dennis
Ottoboni and Han	Art Unit: 1628
Application No.: 15/012,532	Conf. No: 9345
Filed: February 1, 2016	
For: **EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF**	

RESPONSE UNDER 37 C.F.R. § 1.116

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

Commissioner:

The present communication is in response to the final Office Action mailed December 1, 2017, in the above-identified application.

Amendments to the Claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

[The remainder of this page intentionally left blank.]

Amendments to the Claims:

The following listing reflects amendments to the claims and replaces all prior versions and listings of claims in this application.

1.(Previously Presented) An injectable pharmaceutical emulsion comprising:

a neurokinase-1 (NK-1) receptor antagonist;

11 wt/wt% to 15 wt/wt% of an emulsifier;

an oil;

a co-surfactant which comprises an alcohol;

a tonicity agent;

a pH modifier; and

water;

wherein the pH of the emulsion ranges from about 7.5 to 9.0, and the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt%).

2. (Original) The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 5:1 to 15:1 (wt/wt%).

3. (Original) The emulsion according to claim 1, wherein the ratio of the oil to the NK-1 receptor antagonist ranges from about 10:1 to 15:1 (wt/wt%).

4. (Cancelled)

5. (Cancelled)

6. (Original) The emulsion according to claim 1, wherein the ratio of emulsifier to oil ranges from about 1:1 to 3:1 (wt/wt%).

7. (Original) The emulsion according to claim 1, wherein the emulsifier is a phospholipid.

8. (Original) The emulsion according to claim 1, wherein the emulsifier is an egg lecithin.

9. (Original) The emulsion according to claim 1, further comprising dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

10. (Withdrawn) The emulsion according to claim 1, wherein the NK-1 receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, vestipitant, serlopitant, maropitant, casopitant, befetupitant, and orvepitant.

11. (Currently Amended) The emulsion according to claim 1, wherein the pH modifier is ~~an oleate~~ oleic acid or a salt thereof.

12. (Original) The emulsion according to claim 1, wherein the pH modifier is a buffer.

13. (Original) The emulsion according to claim 12, wherein the buffer is Tris buffer.

14. (Original) The emulsion according to claim 1, wherein the oil is soybean oil.

15. (Original) The emulsion according to claim 1, wherein the alcohol is ethanol.

16. (Original) The emulsion according to claim 15, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

17. (Withdrawn) The emulsion according to claim 1, wherein the NK-1 receptor antagonist is not aprepitant.

18. (Withdrawn, Previously Presented) A method for preparing an injectable pharmaceutical emulsion comprising:

(a) combining a NK-1 receptor antagonist, an emulsifier, and an alcohol with an oil to generate an oil phase;

(b) combining water, a tonicity agent, a pH modifier, and optionally a buffer to generate an aqueous phase;

(c) homogenizing the oil phase with the aqueous phase to generate the pharmaceutical emulsion; and

(d) sterilizing the pharmaceutical emulsion.

19. (Withdrawn) The method according to claim 18, wherein step (c) comprises homogenizing the oil phase with the aqueous phase to generate a crude emulsion, and step (c) further comprises homogenizing the crude emulsion to generate a fine emulsion wherein the fine emulsion is the pharmaceutical emulsion.

20. (Withdrawn) The method according to claim 19, wherein homogenizing the crude emulsion comprises using a microfluidizer at a pressure between 10,000 to 30,000 psi.

21. (Withdrawn) The method according to claim 20, wherein homogenizing the crude emulsion comprises 4 to 15 passes through the microfluidizer.

22. (Withdrawn) The method according to claim 18, wherein the sterilizing comprising passing the pharmaceutical emulsion through a filter having a pore size of about 0.2 microns.

23. (Withdrawn) The method according to claim 18, further comprising adding a solution of dexamethasone sodium phosphate to the pharmaceutical emulsion prior to sterile filtration.

24. (Withdrawn) The method according to claim 18, wherein the receptor antagonist is selected from the group consisting of rolapitant, netupitant, ezlopitant, casopitant, befetupitant, vestipitant, serlopitant, maropitant, and orvepitant.

25. (Withdrawn) The method according to claim 18, wherein the NK-1 receptor antagonist is not aprepitant.

26. (Withdrawn) A method for preventing or treating a subject in need thereof, comprising administering to the subject a composition comprising the emulsion according to claim 1.

27. (Withdrawn) The method according to claim 26, wherein the subject is at risk of or is suffering from nausea and/or vomiting.

28. (Withdrawn) The method according to claim 27, wherein the nausea and/or vomiting is induced by chemotherapy, surgery, or radiotherapy.

REMARKS

Consideration of the remarks and amendments presented herein is respectfully requested.

I. Status of the Claims

Without prejudice or disclaimer, claims 4 and 5 were previously cancelled.

Claim 11 is amended herein to more clearly reflect the nature of the claimed subject matter, support for which can be found in the specification as filed, for example, at ¶[0106]. There is no issue of new matter.

Applicants reserve the right to pursue at a later date in one or more continuing applications subject matter supported by the present disclosure, including subject matter which may be considered to be disclaimed herein.

Upon entry of this paper, claims 1-3 and 6-9 and 11-16 are pending and under examination. Claims 10 and 17 are withdrawn for allegedly drawn to non-elected species. Claims 18-28 are withdrawn for allegedly drawn to non-elected groups of claims. Applicants reserve the right to pursue the withdrawn subject matter in a continuing application.

II. Claim Objection

Claim 11 is objected to over the language “an oleate or a salt thereof” because oleate is already a salt. Applicant has amended claim 11 to recite, among other things, “oleic acid or a salt thereof.” Support for the amendments can be found in the application as filed, for example, at ¶[0106]. This objection should be withdrawn.

III. Double Patenting

Claims 1-9, 11, and 14-16 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-11 of US Patent No. 9,561,229. Claims 1-9, 11, and 14-16 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-15 of U.S. Patent No. 9,808,465.

Applicant hereby submits a terminal disclaimer to render moot these double patenting rejections.

IV. Conclusion

The Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-5907.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to contact the undersigned at (650) 815-7399.

Respectfully submitted,
McDermott Will & Emery LLP

Date: February 26, 2018

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NOTICE OF ALLOWANCE AND FEE(S) DUE

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McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DISTRICT OF COLUMBIA 20001

EXAMINER
HEYER, DENNIS

ART UNIT	PAPER NUMBER
1628	

DATE MAILED: 03/12/2018

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/012,532	02/01/2016	Thomas B. Ottoboni	092459-0173/8032	9345

TITLE OF INVENTION: EMULSION FORMULATIONS OF AN NK-1 RECEPTOR ANTAGONIST AND USES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
REGULAR	SMALL	$500	$0.00	$0.00	$500	06/12/2018

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 and an extra copy of the form should be submitted. 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: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (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)

108547 7590 03/12/2018
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DISTRICT OF COLUMBIA 20001

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.

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 facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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REGULAR	SMALL	$500	$0.00	$0.00	$500	06/12/2018

EXAMINER	ART UNIT	CLASS-SUBCLASS
HEYER, DENNIS	1628	514-125000

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/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form 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 _____
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 has been filed for recordation as set forth in 37 CFR 3.11. 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. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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. _____

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

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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 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, 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. 15/012,532	Applicant(s) Ottoboni et al.	
	Examiner DENNIS HEYER	Art Unit 1628	AIA 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 2/26/2018 .
   ☐ 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 1-3 and 6-25 . 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 areply 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 _____ .

/DENNIS HEYER/
Primary Examiner, Art Unit 1628

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

DETAILED ACTION

Acknowledgement is made of Applicant's remarks and amendments in the response filed February 26, 2018. Acknowledgement is made of Applicant's submission of a Terminal Disclaimer on February 26. 2018.

Priority

This application, 15/012,532, was filed 02/01/2016.

Terminal Disclaimer

The terminal disclaimer filed on February 26, 2018 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patent 9,561,229 and US patent 9,808,465 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Withdrawn Objections and Rejections

Claim Objections

The objection to Claim 11 over the language "an oleate or a salt thereof" is rendered moot and is withdrawn in response to Applicant's amendment reciting "wherein the pH modifier is ~~an oleate~~ oleic acid or a salt thereof.

Double Patenting

The rejection of Claims 1 – 9, 11 and 14 – 16 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 – 11 of US patent 9,561,229 and the rejection of Claims 1 – 9, 11 and 14 – 16 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1 – 15 of US patent 9,808,465, are each rendered moot and are withdrawn in response to Applicant's filing of a terminal disclaimer disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US patent 9,561,229 and US patent 9,808,465.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview

with Applicant representative Wen Li on March 2, 2018.

The claims have been amended as follows:

Claims 26 – 28. (Cancelled)

Rejoinder

It is noted that upon the allowance of a generic claim, applicant is entitled to claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. Accordingly, product Claims 10 and 17, previously withdrawn in reply to the response to the election/restriction requirement filed May 19, 2011, are rejoined with the allowed product Claims 1 – 3, 6 – 9 and 11 – 16.

Claims 1 – 3, 6 – 17 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), Claim 18 – 25, directed to the process of making the allowable product, previously withdrawn from consideration as a result of a restriction requirement, April 6, 2017 (i.e. the invention of Group II), are hereby rejoined and fully examined for patentability under 37 CFR 1.104. Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups I and II as set forth in the Office action mailed on November 4, 2016 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over

the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The claimed subject matter drawn to an injectable pharmaceutical emulsion comprising: a neurokinase-1 (NK-1) receptor antagonist; 11 wt/wt% to 15 wt/wt% of an emulsifier; an oil; a co-surfactant which comprises an alcohol; a tonicity agent; a pH modifier; and water; wherein the pH of the emulsion ranges from about 7.5 to 9.0, and the ratio of the emulsifier to the NK-1 receptor antagonist ranges from about 18:1 to 22:1 (wt/wt%), is allowed as being neither anticipated by nor obvious over the closest prior art.

As discussed in the section withdrawing the applied prior art rejections under 35 U.S.C. 103(a), Zhou *et al.* in CN 102379845 (representative of the closest prior art), teach injector teaches emulsion formulations comprising the NK-1 antagonist aprepitant, the emulsifier egg lecithin, the oil, soybean oil, glycerin (a tonicity agent), the alcohol, ethanol and a pH modifier. However, the ratio of emulsifier to aprepitant (the NK-1 antagonist) is significantly below the ratio required by the claimed invention. Accordingly, there would have been no motivation by one of ordinary skill to modify the ratio to those recited by the claimed invention.

Further, as discussed in the Declaration submitted by Thomas Ottoboni (heretofore the “Ottoboni Declaration”) in US application serial No. 15/083,071 (now US patent 9,561,229) cited by Applicant in the Remarks filed 2/26/2018, the claimed

injectable emulsion formulations exhibit surprising and unexpected properties compared to the emulsions of Zhou (Example 4, disclosed in the instant specification) which contains less than 11 wt/wt% of the emulsifier egg yolk lecithin (specifically, 9.95 wt/wt%; outside the scope of the claimed invention) results in crystal formation 4 days after preparation at room temperature. By comparison, Examples 1, 2, 3 and 6 (Table 7, pages 31 – 32 of the present specification) which contain between 11.7 and 14.3 wt/wt% of the emulsifier (within the range recited in instant Claim 1) were stable; i.e. no observable crystal formation after storage at room temperature for at least 2 months.

As such, the claimed emulsion formulations exhibit stability that is surprising and unexpected compared to the closest prior art. See MPEP 716.02(b): Evidence of unexpected properties may be in the form of a direct or indirect comparison of the claimed invention with the closest prior art which is commensurate in scope with the claims. See *In re Boesch,* 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

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."

**It is noted that, in order to further clarify the record, Applicant should submit a copy of the Ottoboni Declaration into the prosecution file history of this application.*

Conclusion

Claims 1 – 3 and 6 – 25 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on 7-7 EST Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, WINSTON SHEN can be reached at (571)272-3157. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/DENNIS HEYER/
Primary Examiner, Art Unit 1628