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Title of Invention:	EMULSION FORMULATIONS OF APREPITANT
First Named Inventor/Applicant Name:	Thomas B. Ottoboni
Customer Number:	108547
Filer:	Susan L. Harlocker/Maria Regina Catiis
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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 C.F.R. Section 1.16 (National application filing, search, and examination fees)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		092459-0170_Application.pdf	1509252 b56b9cc594ee1c750cd07e839a2d1a90ab684890	yes	33

Multipart Description/PDF files in .zip description		
Document Description	**Start**	**End**
Specification	1	30
Claims	31	32
Abstract	33	33

Warnings:					
Information:					
2	Drawings-only black and white line drawings	092459-0170_Figures.pdf	988660 680db3d592fd75d8529bc9474f2bbda79783c107	no	4
Warnings:					
Information:					
3	Oath or Declaration filed	092459-0170_DECLARATION.pdf	109374 490ae306c0b194cf23e7070f337b5ee4196bfc5b	no	2
Warnings:					
Information:					
4	Application Data Sheet	092459-0170_ADS.pdf	269381 1eb0abbccd558a30549ea3c4c75f790e9e26fc02	no	6
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
5	Fee Worksheet (SB06)	fee-info.pdf	35158 a3ab49195e6b019fe5043ea9d8494418484cd1b9	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2911825		

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.

REMARKS

In response to the Notice to file Corrected Application Papers, Applicants have amended the specification as detailed below and are submitting herewith a substitute specification as both a marked up version and a clean copy.

The substitute specification submitted herewith contains no new matter.

The description of FIG. 1 as originally filed on page 9 of the specification is amended to describe FIGS. 1A, 1B, 1C, and 1D. Additionally, paragraphs [0116], [0117], [0118], and [0121] are presently amended to reference FIGS. 1A, 1B, 1C and 1D, respectively. Accordingly, the description complies with 37 C.F.R. § 1.74. Applicants have not amended the Drawings because the Drawings as originally filed are fully described in the specification in compliance with 37 C.F.R. § 1.74 and FIG. 1 is numbered in consecutive Arabic numerals and capital letters in compliance with 37 C.F.R. § 1.84(u)(1).

I. Amendments to the Specification

Paragraph [0060] on page 9 of the specification as filed is amended to refer to the individual views of FIG. 1A, 1B, 1C and 1D and to provide a period at the end of the sentence.

Paragraph [0116] on page 21 of the specification as filed is amended to refer to FIG. 1A.

Paragraph [0117] on page 22 of the specification as filed is amended to refer to FIG. 1B.

Paragraph [0118] on page 23 of the specification as filed is amended to refer to FIG. 1C.

Paragraph [0121] on page 26 of the specification as filed is amended to refer to FIG. 1D.

No new matter is added by way of these amendments.

II. Conclusion

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

If the office has any questions or believes a telephone conference would expedite grant, the Office is encouraged to call the undersigned at (650) 815-7647.

Respectfully submitted,
McDermott Will & Emery LLP

Date: October 23, 2015

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

Correspondence
Customer No. 108547

WHAT IS CLAIMED IS:

1. An injectable emulsion comprising:

aprepitant;

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

an oil;

a co-emulsifier which is an alcohol;

a tonicity modifier;

a pH modifier; and

water;

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

2. The emulsion according to claim 1, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt%).

3. The emulsion according to claim 1, wherein the ratio of the emulsifier to the aprepitant within the oil phase of the emulsion ranges from about 15:1 to 30:1 (wt/wt%).

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

5. The emulsion according to claim 4, wherein the emulsifier is a phospholipid.

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

7. The emulsion according to claim 1, wherein the emulsifier is an egg lecithin.

8. The emulsion according to claim 1, further comprising a buffer.

9. The emulsion according to claim 1, wherein the pH modifier is sodium oleate.

10. The emulsion according to claim 8, wherein the buffer is Tris buffer.

11. The emulsion according to claim 1, wherein the oil is soybean oil.

12. The emulsion according to claim 1, wherein the alcohol is ethanol.

13. The emulsion according to claim 12, wherein the ethanol is present at less than 10 wt/wt%.

14. A method for preparing a pharmaceutical emulsion comprising:

combining aprepitant, an emulsifier, and an alcohol with an oil to generate an oil phase;

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

homogenizing the oil phase with the aqueous phase to generate a coarse emulsion premix;

homogenizing the coarse emulsion premix at a pressure between 10,000 and 30,000 psi using a microfluidizer to generate the pharmaceutical emulsion; and

sterilizing the pharmaceutical emulsion.

15. The method according to claim 14, wherein homogenizing the coarse emulsion premix comprises 4 to 15 passes through the microfluidizer.

16. The method according to claim 14, wherein the sterilizing comprising passing the pharmaceutical emulsion through a filter having a pore size of about 0.2 microns.

17. The method according to claim 14, further comprising adding a solution of dexamethasone sodium phosphate to the fine emulsion prior to sterile filtration.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Thomas B. Ottoboni	Examiner:	Miriam A. Levin
Application No.:	14/859,013	Art Unit:	1613
Filed:	September 18, 2015	Conf. No:	7185
For:	**EMULSION FORMULATIONS OF APREPITANT**		

PRELIMINARY AMENDMENT

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

Sir:

Prior to examination of the above-referenced patent application on its merits, please enter the following amendments.

Amendments to the Specifications begin on page 2.

Amendments to the Claims begin on page 3.

Remarks begin on page 6.

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 emulsion comprising:

aprepitant;

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

an oil;

a co-emulsifier which is an alcohol;

a tonicity modifier;

a pH modifier; and

water;

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

2. (Previously presented) The emulsion according to claim 1, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt%).

3. (Previously presented) The emulsion according to claim 1, wherein the ratio of the emulsifier to the aprepitant within the oil phase of the emulsion ranges from about 15:1 to 30:1 (wt/wt%).

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

5. (Previously presented) The emulsion according to claim 4, wherein the emulsifier is a phospholipid.

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

7. (Previously presented) The emulsion according to claim 1, wherein the emulsifier is an egg lecithin.

8. (Previously presented) The emulsion according to claim 1, further comprising a buffer.

9. (Previously presented) The emulsion according to claim 1, wherein the pH modifier is sodium oleate.

10. (Previously presented) The emulsion according to claim 8, wherein the buffer is Tris buffer.

11. (Previously presented) The emulsion according to claim 1, wherein the oil is soybean oil.

12. (Previously presented) The emulsion according to claim 1, wherein the alcohol is ethanol.

13. (Previously presented) The emulsion according to claim 12, wherein the ethanol is present at less than 10 wt/wt%.

14. (Previously presented) A method for preparing a pharmaceutical emulsion comprising:

combining aprepitant, an emulsifier, and an alcohol with an oil to generate an oil phase;

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

homogenizing the oil phase with the aqueous phase to generate a coarse emulsion premix;

homogenizing the coarse emulsion premix at a pressure between 10,000 and 30,000 psi using a microfluidizer to generate the pharmaceutical emulsion; and

sterilizing the pharmaceutical emulsion.

15. (Previously presented) The method according to claim 14, wherein homogenizing the coarse emulsion premix comprises 4 to 15 passes through the microfluidizer.

16. (Previously presented) The method according to claim 14, wherein the sterilizing comprising passing the pharmaceutical emulsion through a filter having a pore size of about 0.2 microns.

17. (Previously presented) The method according to claim 14, further comprising adding a solution of dexamethasone sodium phosphate to the fine emulsion prior to sterile filtration.

18. (New) 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.

19. (New) The method according to claim 18, wherein the subject is at risk of or is suffering from emesis.

20. (New) The method according to claim 18, wherein the emesis is induced by chemotherapy.

REMARKS

Entry of this Preliminary Amendment prior to examination of the claims is respectfully requested. Amendments to the specification claims are provided herein.

I. Amendments to the Specification

Paragraph [0043] on page 7 of the specification as filed is amended to correct a clerical error. Specifically, this paragraph as originally filed recites in part a composition which is a stable system maintaining an intensity-weighted mean particle size as determined by dynamic light scattering above 500 nm and further recites in part that the average droplet size is maintained above 500 nm for a period of at least 1 month, 3 months, etc. Applicants respectfully request that paragraph [0043] be amended to replace "above 500 nm" with "below 500 nm."

Applicants assert that this amendment to paragraph [0043] is clearly clerical in nature in view of what is known to the person having ordinary skill in the art. Support for this assertion lies at least in paragraph [0006] on page 2 of the originally filed specification (emphasis added):

> **[0006]** Intravenous emulsions should have a very small droplet size to circulate in the bloodstream without causing capillary blockage and embolization. **These size limits are typified by USP33-NF28 General Chapter <729> for Globule Size Distribution in Lipid Injectable Emulsions, hereinafter referred to as USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm** and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm (PFAT5) not exceeding 0.05%, irrespective of the final lipid concentration.

Applicants also refer to paragraph [0068] on page 10 of the specification as filed (emphasis added):

> **[0068] "Physically stable" emulsions will meet the criteria under USP <729>, which defines universal limits for (1) mean droplet size not exceeding 500 nm or 0.5 μm** and (2) the population of large-diameter fat globules, expressed as the volume-weighted percentage of fat greater than 5 μm

(PFAT5) not exceeding 0.05%, at 5 °C or room temperature for a designated storage time period. In addition, physically stable emulsions will have no visible aprepitant crystals upon storage at 5 °C or room temperature for a designated time period. Crystals are considered visible when viewed at magnification of 4X to 10X. An emulsion is physically stable if it meets the criteria under USP <729> and aprepitant crystals are not visible upon storage at 5 °C or room temperature for a time period equal to or at least 1 week, 2 weeks, 4 weeks, 1 month, 2 months, 6 months, 1 year or 2 years.

No new matter is added by way of these amendments to the specification.

II. Amendments to the Claims

New claims 18-20 are added and recite methods for treating subjects. Support can be found throughout the specification including, for example, paragraphs [0113-0115] on pages 20-21 of the specification as filed.

No new matter is added by way of these amendments to the claims.

III. Conclusion

If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 815-7647.

Respectfully submitted,
McDermott Will & Emery LLP

Date: February 16, 2016

Susan L. Harlocker
Reg. No. 59,144

Correspondence
Customer No. 108547

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/859,013	09/18/2015	Thomas B. Ottoboni	092459-0170/8027.US00	7185

108547 7590 06/06/2016

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER
LEVIN, MIRIAM A

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
06/06/2016	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. 14/859,013	Applicant(s) OTTOBONI ET AL.	
	Examiner MIRIAM A. LEVIN	Art Unit 1613	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 *February 16, 2016*.

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

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

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

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

Disposition of Claims*

5)☒ Claim(s) *1 - 20* is/are pending in the application.

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

6)☐ Claim(s) _____ is/are allowed.

7)☐ Claim(s) _____ is/are rejected.

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

9)☒ Claim(s) *1 -20* 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: _____.

1. 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

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

I. Claims 1 - 13, drawn to an injectable emulsion comprising aprepitant, classified in A61K 31/5377.

II. Claim 14 - 17, drawn to a process of making an emulsion, classified in A61K 9/107

III. Claims 18 – 20, drawn to a method of treatment, classified in A61K 9/0019.

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

3. Inventions I and II 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 emulsions can also be prepared using a colloid mill. (See, University of North Carolina, The Pharmaceutics and Compounding Laboratory, Emulsions: Preparation and Stabilization, Methods of Emulsion Preparation, [Retrieved from internet <URL: http://pharmlabs.unc.edu/labs/emulsions/prep.htm >], [Downloaded May 26, 2016], 1 page.)

4. Inventions I and III 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 method claims merely recite "preventing or treating a subject in need thereof" and "administering," therefore any method of treating any subject for any condition is an alternative treatment method.

5. Inventions II and III are directed to related processes. 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 are a process of making and a process of using, therefore they have materially different design, mode of operations, function and effect. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

6. 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 one or more of the following reasons apply:

The species or groupings of patentably indistinct species have acquired a separate status in the art in view of their different classification.

The species or groupings of patentably distinct species require a different field of search (e.g. searching different class/subclasses or electronic resources, or employing different search strategies or search queries).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of an 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 or pre-AIA 35 U.S.C. 103(a) of the other invention.

7. This application contains claims directed to the following patentably distinct species. Please elect one species for each set below, regardless of the invention selected above:

a. An emulsifier, e.g. egg lecithin (cl. 7);

b. An oil, e.g. soybean oil (cl. 11);

c. A co-emulsifier, e.g. ethanol (cl. 12)

d. A tonicity modifier, e.g. sucrose (e.g. spec. p. 15, [0091]);

e. A pH modifier, e.g. sodium oleate (cl. 9);

f. A buffer, e.g. Tris buffer (cl. 8, 10).

8. The species are independent or distinct because different compounds have different structures and different physical and chemical properties. 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 a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 is generic.

There is a search and/or examination burden for the patentably distinct species as set forth above because at least the following reason(s) apply:

The species or groupings of patentably indistinct species have acquired a separate status in the art in view of their different classification.

The species or groupings of patentably indistinct species have acquired a separate status in the art due to their recognized divergent subject matter.

The species or groupings of patentably distinct species require a different field of search (e.g. searching different class/subclasses or electronic resources, or employing different search strategies or search queries).

The different compounds which could be used for each claimed element have different structures and properties, therefore they are classified in different classes and searches for one species may not produce art reading on other species.

Moreover, attempting to search for all of the possible combinations of compounds will be very time consuming and may produce a vast sea of references that will take hours or days for the Examiner to review. This imposes a significant burden on the Examiner.

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 or grouping of patentably indistinct 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 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 or grouping of patentably indistinct species.

Should applicant traverse on the ground that the species, or groupings of patentably indistinct species from which election is required, are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing them 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 or pre-AIA 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.

9. A telephone call was made to Susan Harlocker, Reg. No. 59,144, on May 24, 2016 to request an oral election to the above restriction requirement, but did not result in an election being made.

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be corrected in compliance with 37 CFR 1.48(a) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. A request to correct inventorship under 37 CFR 1.48(a) must be accompanied by an application data sheet in accordance with 37 CFR 1.76 that identifies each inventor by his or her legal name and by the processing fee required under 37 CFR 1.17(i).

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

In the event of rejoinder, the requirement for restriction between the product/apparatus 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/apparatus are found allowable, an otherwise proper restriction requirement between product/apparatus claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product/apparatus claim will not be rejoined. See MPEP § 821.04. Additionally, in order for rejoinder to occur, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product/apparatus claims. **Failure to do so may result in no 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.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MIRIAM A. LEVIN whose telephone number is (571)270-3471. The examiner can normally be reached on 11 am - 7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon can be reached on 571-272-0581. 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.

/M. A. L./
Examiner, Art Unit 1613

/ANNA PAGONAKIS/

Primary Examiner, Art Unit 1628

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Thomas B. Ottoboni et al.	Examiner:	Miriam A. Levin
Application No.:	14/859,013	Art Unit:	1613
Filed:	September 18, 2015	Conf. No:	7185
For:	**EMULSION FORMULATIONS OF APREPITANT**		

RESPONSE TO RESTRICTION REQUIREMENT

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

Sir:

The present communication responds to the Restriction Requirement dated June 6, 2016 in the above-referenced patent application.

Amendments to the Claims begin on page 2.

Remarks begin on page 4.

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.-17. (Canceled)

18. (Currently amended) A method for preventing or treating a subject at risk of or is suffering from emesis ~~in need thereof~~, comprising administering to the subject a composition comprising an injectable emulsion wherein the emulsion comprises:

aprepitant;

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

an oil;

a co-emulsifier which is an alcohol;

a tonicity modifier;

a pH modifier; and

water;

wherein the pH of the emulsion ranges from about 7.5 to 9.0 ~~the emulsion according to claim 1~~.

19. (Canceled)

20. (Previously presented) The method according to claim 18, wherein the emesis is induced by chemotherapy.

21. (New) The method according to claim 18, wherein the emesis is induced by highly emetogenic chemotherapy.

22. (New) The method according to claim 18, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt%).

23. (New) The method according to claim 18, wherein the ratio of the emulsifier to the aprepitant within the oil phase of the emulsion ranges from about 15:1 to 30:1 (wt/wt%).

24. (New) The method according to claim 18, wherein the ratio of emulsifier to oil ranges from about 1:1 to 3:1 (wt/wt%).

25. (New) The method according to claim 24, wherein the emulsifier in the emulsion is a phospholipid.

26. (New) The method according to claim 18, wherein the emulsion further comprises dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

27. (New) The method according to claim 18, wherein the emulsifier in the emulsion is an egg lecithin.

28. (New) The method according to claim 18, wherein the pH modifier in the emulsion is sodium oleate.

29. (New) The method according to claim 18, wherein the emulsion further comprises a buffer.

30. (New) The method according to claim 29, wherein the buffer is Tris buffer.

31. (New) The method according to claim 18, wherein the oil in the emulsion is soybean oil.

32. (New) The method according to claim 18, wherein the alcohol in the emulsion is ethanol.

33. (New) The method according to claim 32, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

34. (New) The method according to claim 32, wherein the tonicity modifier in the emulsion is sucrose.

REMARKS

Consideration of the remarks presented herein is respectfully requested.

Status of the Claims

Claims 1-20 are pending. With this amendment, claim 18 is amended, new claims 21-34 are added and claims 1-17 and 19 are canceled.

Applicant reserves 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.

Amendments to the Claims

Claim 18 is amended to recite emesis. Support is found at least in claim 19 as originally filed.

Claims 18 is further amended to recite the elements of claim 1.

New claim 21 recites wherein the emesis is induced by highly emetogenic chemotherapy. Support can be found, for example, in the Abstract as originally filed.

New claims 22-34 recite subject matter recited in claims 2-13 as originally filed.

Claims 1-17 and 19 are canceled.

No new matter is added by way of these amendments.

Group Elections

In the Office Action, the Examiner divided the claims into the following groups:

Group I.	Claims 1-13, drawn to an injectable emulsion comprising aprepitant, classified in A61K31/5377.
Group II.	Claim 14-17, drawn to a process of making an emulsion, classified in A61K 9/107.
Group III.	Claims 18-20, drawn to a method of treatment, classified in A61K 9/0019.

In response, Applicants elect Group III, claims 18-20 without traverse. With this response, the claims are amended to add new claims 21-34 and cancel claim 19. Claims 18 and 20-34 read upon the elected group.

Species Elections

The Examiner further required election of species. Applicants respond as follows:

a. An emulsifier: Applicants elect egg lecithin; claims 18 and 20-34 read upon the elected species.

b. An oil: Applicants elect soybean oil; claims 18 and 20-34 read upon the elected species.

c. A co-emulsifier: Applicants elect ethanol; claims 18 and 20-34 read upon the elected species.

d. A tonicity modifier: Applicants elect sucrose; claims 18 and 20-34 read upon the elected species.

e. A pH modifier: Applicants elect sodium oleate; claims 18 and 20-34 read upon the elected species.

f. A buffer: Applicants elect Tris buffer; claims 28 and 30 read upon the elected species.

Conclusion

No fees are believed due with this communication. However, the Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-5907. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 815-7647.

Respectfully submitted,
McDermott Will & Emery LLP

Date: July 22, 2016

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

Correspondence
Customer No. 108547

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/859,013	09/18/2015	Thomas B. Ottoboni	092459-0170/8027.US00	7185

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McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER	
LEVIN, MIRIAM A	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
11/18/2016	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. 14/859,013	Applicant(s) OTTOBONI ET AL.	
	Examiner MIRIAM A. LEVIN	Art Unit 1613	AIA (First Inventor to File) Status Yes

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

Period for Reply

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

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

Status

1)☒ Responsive to communication(s) filed on *July 22, 2016*.

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

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

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

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

Disposition of Claims*

5)☒ Claim(s) *18, 20 - 34* 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) *18, 20 - 34* is/are rejected.

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

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

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

Application Papers

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

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

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

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

Priority under 35 U.S.C. § 119

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

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

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

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

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

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

Attachment(s)

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

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

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

4) ☐ Other: _____.

1. 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

2. Applicant's amendment filed July 22, 2016 has been received and entered.

Status of Claims

3. Claims Pending: 18 and 20 - 34
4. New claims: 2 - 34
5. Amended claims: 18
6. Canceled Claims: 1 - 17, 19
7. Withdrawn claims: none
8. Change in Dependency: Claim 18 converted to independent claim.

9. Elected group: III (method of treatment)
10. Elected species:
    a. Emulsifier – egg lecithin
    b. Oil = soybean oil
    c. Co-emulsifier = ethanol
    d. Tonicity modifier = sucrose
    e. pH modifier = sodium oleate
    f. buffer = TRIS

11. Objections/Rejections withdrawn: N/A

12. Rejections maintained with revision: N/A

13. New Grounds and/or Rejections necessitated by amendment:
    g. 35 USC 103 over Zhou (CN 102379845 A) vs. cl. 18 and 20 - 25, 27 and 31 – 34
    h. 35 USC 103 over Zhou + Hargreaves + Sun vs. cl. 26
    i. 35 USC 103 over Zhou + Karavas + Bromer + Wan vs. cl. 28 – 30
    j. NSDP (ODP) vs. 15/083071

14. Terminal Disclaimers: None

15. Applicant's arguments filed July 22, 2016 have been fully considered. The following rejections constitute the complete set of rejections presently being applied to the instant application.

Election/Restrictions

16. Applicant's election without traverse of the invention of Group III, the method of making, and the species indicated above, in the reply filed on July 22, 2016 is acknowledged.

Information Disclosure Statement

17. There appeared to be a typographical error on the IDS submitted on February 23, 2016. The Examiner assumed the cited references were intended to include those cited on the international search

report cited on the IDS and corrected the IDS accordingly. If the reference indicated by the Examiner is incorrect, please double check the publication number and cite the reference again.

Claim Rejections - 35 USC § 103

18. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

19. 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.

20. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. Claims 18 and 20 - 25, 27 and 31 - 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR). (Note: English translation is attached to the back of the Chinese publication. Citation is made to the English translation.)

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the

examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

23. Applicant claims a method of treating a patient at risk of or suffering from emesis comprising administration of an injectable pharmaceutical emulsion comprising:

k. aprepitant;

l. 11 – 15 wt. % emulsifier (elected species egg yolk lecithin);

m. Oil (elected species soybean oil);

n. Co-emulsifier which is an alcohol (elected species ethanol);

o. Tonicity modifier (elected species sucrose);

p. pH modifier (elected species sodium oleate);

q. water;

r. Wherein the emulsion has a pH of 7.5 – 9.0.

Determination of the scope and content of the prior art (MPEP 2141.01)

24. Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. (title)

25. Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003]) CINV is chemotherapy-induced nausea and vomiting.

26. The emulsion comprises, for example:

s. 0.5 - 2.0 wt. % aprepitant, preferably 1.0 - 1.5 wt. %;

t. 0.5 – 10 wt. % emulsifier; preferably 8 – 10 wt. %, wherein the emulsifier is egg yolk phospholipids;

u. 5 – 30 wt. % oil, preferably 7 – 15 wt. % oil, wherein the oil is soybean oil;

v. 1 – 10 wt. % co-emulsifier, preferably 7 – 13 wt. % co-emulsifier; alternatively, preferably 2 – 5 wt. %, wherein the co-emulsifier is ethanol;

w. 5 – 20 wt. % of a protective agent (compare vs. tonicity modifier of instant claims), preferably 8 – 13 wt. %, wherein the protective agent may be glycerin, sucrose or glucose;

x. 60 – 80 wt. % water, preferably 60 – 69 wt. %;

y. Wherein the pH of the microemulsion is 6.0 - 8.0.

z. (See, e.g. cl. 1, 5 – 9; [0008] – [0011]; see also examples).

27. Zhou et al. teach the emulsion may then be lyophilized for later use. (e.g. [0026])

28. Zhou et al. teach that the emulsion may be concentrated into small-volume injection vials. For example, in Ex. 5, 115 mg aprepitant emulsion is placed in a 5 mL vial. The starting emulsion has 2 grams of aprepitant. 2 grams / 0.115 grams = 17.39 aliquots. If each aliquot is 5 mL, that only accounts for 86 mL, which is probably not the entire volume. (See, [0028])

29. In Ex. 6, the emulsion comprises 0.5 g aprepitant, and each 5 mL aliquot comprises 150 mg; or nearly 1/3 of the total. (See, e.g. [0029], [0030]) Clearly this emulsion must have been concentrated prior to being placed in the 5 mL vial.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

30. The difference between the instant application and Zhou et al. is that Zhou et al. do not expressly teach a weight percent of emulsifier greater than 10 wt. %, however Zhou et al. teach that the emulsion may be lyophilized or otherwise concentrated to be placed in vials and other containers for future use.

Finding of prima facie obviousness Rationale and Motivation (MPEP 2142-2143)

31. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use 11 – 15 wt. % emulsifier, as suggested by Zhou et al., and produce the instant invention.

32. One of ordinary skill in the art would have been motivated to do this because Zhou et al. teach up to 10 wt. % and teach the emulsion may be concentrated or lyophilized prior to use. Therefore this is merely a dilution / concentration step, i.e., a change in size or proportion, which is within the teachings of Zhou and is therefore obvious.

33. Even if, arguendo it is determined that this concentration change is not within the teaching of Zhou, it is a change in size or proportion and is therefore obvious per (MPEP 2144.04 (IV) (A).

34. Alternatively, there is no indication that the difference between 10 wt. % of Zhou and 11 wt. % of the instant claims makes a material difference in the composition; therefore this is an obvious variant that is arrived at by routine optimization.

35. In regard to the ratios and other ranges recited in the instant claims, these limitations overlap those of Zhou et al. and are therefore anticipated (MPEP 2131.03) or obvious per MPEP 2144.05:

2131.03Anticipation of Ranges [R-6]

I. A SPECIFIC EXAMPLE IN THE PRIOR ART WHICH IS WITHIN A CLAIMED RANGE ANTICIPATES THE RANGE

"[W]hen, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art." *Titanium Metals Corp. v. Banner,* 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (citing *In re Petering*, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)) (emphasis in original)

2144.05 Obviousness of Ranges [R-5]

I. OVERLAP OF RANGES

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, 191USPQ 90 (CCPA 1976) . . . Similarly, 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) . . .

Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal wt. % of emulsifier needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of the wt. % of emulsifier would have been obvious at the time of Applicant's invention.

36. In regard to prevention or treatment of emesis, e.g. induced by chemotherapy, Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003]) (NOTE: CINV is chemotherapy-induced nausea and vomiting.)

37. In regard to the aprepitant being present in the oil phase (instant cl. 23), because the compositions are comprised of the same compounds, the composition will have the same chemical and physical properties.

"A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

38. Claims 18 and 20 - 25, 27 and 31 - 34 are rejected.

39. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

40. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Zhou + Hargreaves + Sun

41. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR), in view of Hargreaves et al. (Development of aprepitant, the first neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting, Annals of the New York Academy of Sciences (Ann. N.Y. Acad. Sci.) (2011) 1222: 40-48 (Issue: Pharmaceutical Science to Improve the Human Condition: Prix Galien, 2010), and Sun et al. (Compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids, Cancer Chemother. Pharmacol. (2013) (available on-line July 17, 2013) 72: 509 - 513).

Determination of the scope and content of the prior art (MPEP 2141.01)

42. As discussed above, Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003])

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

43. The difference between the instant application and Zhou et al. is that Zhou et al. do not expressly teach the composition further comprising dexamethasone sodium phosphate. This deficiency in Zhou et al. is cured by the teachings of Hargreaves et al. and Sun et al.

44. Hargreaves et al. teach development of aprepitant, the first neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting (CINV) where "[a]prepitant, in combination

with a 5-HT3 receptor antagonist and dexamethasone, optimizes protection against CINV in both the acute and delayed phases compared to the prior standard of care, and is now recommended as the first-line therapy for patients about to be treated with moderately or high emetogenic chemotherapy." (title, abstract, conclusion)

45. Sun et al. teach "Compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids," wherein dexamethasone sodium phosphate is one of two corticosteroids tested, "Fosaprepitant demonstrated compatibility when combined in the same IV infusion bag with common 5-HT3 antagonists and corticosteroids for storage and IV administration . . ." and "[u]se of fosaprepitant in combination with other antiemetics may provide a flexible option for administration of antiemetics to patients receiving moderately or highly emetogenic chemotherapy."(Title, Abs.)

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

46. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use dexamethasone sodium phosphate in the aprepitant composition to treat CINV, as suggested by Zhou et al., Hargreaves et al., and Sun et al., and produce the instant invention.

47. One of ordinary skill in the art would have been motivated to do this because all three references teach aprepitant to treat CINV (chemotherapy induced nausea and vomiting), Hargreaves et al. teach aprepitant plus dexamethasone and a 5-HT3 antagonist as first-line therapy for CINV, and Sun et al. teach dexamethasone sodium phosphate as a form of the drug that is compatible with aprepitant for IV administration. The combination of references provide strong motivation to use the two drugs in combination to treat CINV, and to use the sodium phosphate salt as a preferred form of dexamethasone.

48. Claim 26 is rejected.

49. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

50. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as

a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Zhou + Karavas + Bromer + Wan

51. Claims 28 - 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR) (cited above), in view of Karavas et al. (WO 2014/005606 A1; cited on IDS and ISR), Bromer et al. (US 2007/0071777 A1; cited on IDS) and Wan et al. (US 2016/0024092 A1; cited on IDS and ISR).

Determination of the scope and content of the prior art (MPEP 2141.01)

52. As discussed above, Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. (title) The emulsion comprises, for example:

aa. 0.5 - 2.0 wt. % aprepitant, preferably 1.0 - 1.5 wt. %;

bb. 5 – 30 wt. % oil, preferably 7 – 15 wt. % oil, wherein the oil is soybean oil;

cc. 0.5 – 10 wt. % emulsifier; preferably 8 – 10 wt. %, wherein the emulsifier is egg yolk phospholipids;

dd. 1 – 10 wt. % co-emulsifier, preferably 2 – 5 wt. %, wherein the co-emulsifier is ethanol;

ee. 5 – 20 wt. % of a protective agent, preferably 8 – 13 wt. %, wherein the protective agent may be glycerin, sucrose or glucose;

ff. 60 – 80 wt. % water, preferably 60 – 69 wt. %;

gg. Wherein the pH of the microemulsion is 6.0 - 8.0.

hh. (See, e.g. cl. 1, 5 – 9; [0008] – [0011]; see also examples).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

53. The difference between the instant application and Zhou et al. is that while Zhou et al. teach emulsifiers and a desired pH, Zhou et al. do not expressly teach sodium oleate or buffers, such as TRIS. These deficiencies in Zhou et al. are cured by the teachings of Karavas et al., Bromer et al. and Wan et al.

54. Karavas et al. teach stable injectable pharmaceutical compositions of neurokinin 1 receptor antagonist and process for preparation thereof. (Title) The neurokinin 1 receptor antagonist is preferable Aprepitant. (Abs.) The composition comprises 0.01 - 50 wt. % of solubilizing or wetting agents, such as sodium oleate (e.g., p. 4, l. 41 - p. 5, l. 8; p. 6, l. 48 - p. 7, l. 8; p. 9, ll. 28- 37; cl. 9,). The composition has a pH of about 6 to about 8, preferably about 7, which can optionally be obtained using a buffer; the pH adjusters may be acids or acid salts and may have sodium as the counterion / salt. (e.g. p. 5, ll. 19 - 25; p. 6, ll. 41 - 46; p. 7, ll. 30 – 38; p. 9, ll. 20 – 21; p. 9, ll. 39 – 47; cl. 9).

55. Bromer et al. teach an oil emulsion for postnatal hormone substitution (title). The composition may be administered intravenously and may be administered to premature babies. (abs.) An example of the composition comprises soybean oil, egg yolk lecithin (phospholipids), glycerol, water, and sodium oleate. (e.g. [0059], Table 1; see also, e.g., [0037], [0047], [0058]). The pH is adjusted to 6.0 to 9.0 and sodium oleate may be used to adjust the pH of the oil in water emulsion. (e.g. [0053], [0058])

56. Wan et al. teach intravenous formulations of neurokinin-1 antagonists. (Title) Wan et al. teach that TRIS is a suitable buffer for a pH of 7 - 8. (e.g. [0130])

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

57. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use sodium oleate or TRIS buffer in the composition, as suggested by Zhou et al., Bromer et al., and Wan et al., and produce the instant invention.

58. One of ordinary skill in the art would have been motivated to do this because Zhou et al. teach a desired pH of 6 – 8, but do not recite any particular agent as preferred for adjusting the pH, therefore any suitable compounds may be used. Karavas et al. teach that sodium oleate and buffers may be used in injectable formulations of aprepitant. Bromer et al. teach that sodium oleate may be used a pH adjuster to obtain a pH of 6 - 9, and Wan et al. teach that TRIS may be used to obtain a pH of 7 - 8.

59. In the absence of unexpected results or other evidence to the contrary, the selection of sodium oleate or TRIS buffer is the mere selection of a material suitable for the intended use. (MPEP 2144.07)

60. As a second motivation, it is well known in chemistry that use of buffer solutions can provide a more stable or resilient pH. Buffer solutions are formed by using both acid and base, or the salt of an acid. Sodium oleate is the acid salt of oleic acid and sodium hydroxide. Soybean oil contains oleic acid, therefore by using sodium oleate to adjust the pH of the composition, a buffered solution (emulsion) is obtained. This provides additional motivation for the selection of sodium oleate, and assurance of predictable results.

61. TRIS buffer is already a buffer solution; therefore it also provides the more stable pH obtained with a buffered solution.

62. As further motivation in regard to the selection of sodium oleate, and assurance of predictable results / reasonable expectation of success: the composition of Bromer is an oil-in-water emulsion, as is the one of Zhou. Both comprise soybean oil and egg yolk lecithin and both compositions may be injected; the composition of Bromer may be injected in infants. Because both compositions are oil-in-water emulsions, both use similar aqueous phases (glycerol and water), oil phases (soybean oil) and emulsifiers (egg yolk lecithin); and both are intended for use as injectable compositions, use of the same pH adjuster (sodium oleate) is an obvious option and, because of the similarity in the compositions, there is a reasonable expectation of success.

63. The following motivations apply:

2141>Examination Guidelines for Determining Obviousness Under < 35 U.S.C. 103 [R-6]**

III. RATIONALES TO SUPPORT REJECTIONS UNDER 35 U.S.C. 103

(A)Combining prior art elements according to known methods to yield predictable results;
(B)Simple substitution of one known element for another to obtain predictable results;
(E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
(G)Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

64. Claims 28 – 30 are rejected.

65. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

66. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

67. 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).

68. 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).

69. 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.

70. Claims 18 and 20 - 34 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1 – 21 of copending Application No. 15/083,071 (the '071). Although /the claims at issue are not identical, they are not patentably distinct from each other because the instant claims recite a method for treating nausea and vomiting, due, e.g. to chemotherapy, comprising administering an injectable pharmaceutical emulsion comprising:

ii. aprepitant;

jj. 11 – 15 wt. % emulsifier (elected species egg yolk lecithin);

kk. Oil (elected species soybean oil);

ll. Co-emulsifier which is an alcohol (elected species ethanol, up to 10 wt. %);

mm. Tonicity modifier (elected species sucrose);

nn. pH modifier (elected species sodium oleate);

oo. water;

pp. optional buffer, e.g. TRIS;

qq. Wherein the emulsion has a pH of 7.5 – 9.0, and wherein there may be specific ratios of emulsifier to oil and ratios of oil or emulsifier to aprepitant.

71. Copending claims 1 - 11 recite a composition comprising 0.4 - 1.0 wt. % aprepitant, 13 - 15 wt. % egg yolk lecithin, 9 - 10 wt. % soybean oil, sodium oleate as a pH modifier, a pH of 7.5 - 9.0; 3 – 8 wt. % sucrose and 2 – 6 wt. % ethanol, and narrower ranges falling within these (cl. 1 - 11). Copending claims 12 – 21 recite a method of treatment comprising administering the composition, including intravenous administration, for treatment of nausea and vomiting caused by chemotherapy. (cl. 12 - 21)

72. In regard to the any difference in ranges:

2144.05 Obviousness of Ranges [R-5]

I. OVERLAP OF RANGES

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, 191USPQ 90 (CCPA 1976) . . . Similarly, 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) (Court held as proper a rejection of a claim directed to an alloy of "having 0.8% nickel, 0.3%molybdenum, up to 0.1% iron, balance titanium" as obvious over a reference disclosing alloys of 0.75%nickel, 0.25% molybdenum, balance titanium and 0.94%nickel, 0.31% molybdenum, balance titanium.).

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

Claims 18 and 20 - 34 are rejected. No claims are allowed.

Any inquiry regarding this communication or earlier communications from the examiner should be directed to Miriam Levin whose telephone number is 571-270-3471. The examiner can normally be reached between the hours of 10:00 AM - 6:30 PM, EST, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon can be reached at 571-272-0581. The fax number for the organization where this application or proceeding is assigned is 571-273-4371.

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 any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/M. A. L./

Examiner, Art Unit 1613

/ANNA PAGONAKIS/

Primary Examiner, Art Unit 1628

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Thomas B. Ottoboni et al.	Examiner:	Miriam A. Levin
Application No.:	14/859,013	Art Unit:	1613
Filed:	September 18, 2015	Conf. No:	7185
For:	**EMULSION FORMULATIONS OF APREPITANT**		

AMENDMENT 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 responds to the non-final Office action dated November 18, 2016 in the above-referenced patent application. With this response, Applicant petitions for a two-month extension of time to extend the due date for responding to and including April 18, 2017.

Amendments to the Specification begin on page 2.

Amendments to the Claims begin on page 3.

Remarks begin on page 5.

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.-17. (Canceled)

18. (Currently amended) A method for preventing or treating a subject at risk of or [[is]] suffering from emesis, comprising administering to the subject a composition comprising an injectable emulsion wherein the emulsion comprises:

aprepitant;

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

an oil;

a co-emulsifier which is an alcohol;

a tonicity modifier;

a pH modifier; and

water;

wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1, and

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

19. (Canceled)

20. (Previously presented) The method according to claim 18, wherein the emesis is induced by chemotherapy.

21. (Previously presented) The method according to claim 18, wherein the emesis is induced by highly emetogenic chemotherapy.

22. (Previously presented) The method according to claim 18, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt%).

23. (Canceled)

24. (Previously presented) The method according to claim 18, wherein the ratio of emulsifier to oil ranges from about 1:1 to 3:1 (wt/wt%).

25. (Previously presented) The method according to claim 24, wherein the emulsifier in the emulsion is a phospholipid.

26. (Previously presented) The method according to claim 18, wherein the emulsion further comprises dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

27. (Previously presented) The method according to claim 18, wherein the emulsifier in the emulsion is an egg lecithin.

28. (Previously presented) The method according to claim 18, wherein the pH modifier in the emulsion is sodium oleate.

29. (Previously presented) The method according to claim 18, wherein the emulsion further comprises a buffer.

30. (Previously presented) The method according to claim 29, wherein the buffer is Tris buffer.

31. (Previously presented) The method according to claim 18, wherein the oil in the emulsion is soybean oil.

32. (Previously presented) The method according to claim 18, wherein the alcohol in the emulsion is ethanol.

33. (Previously presented) The method according to claim 32, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

34. (Previously presented) The method according to claim 32, wherein the tonicity modifier in the emulsion is sucrose.

REMARKS

Consideration of the remarks presented herein is respectfully requested.

I. Status of the Claims

Claims 18 and 20-34 are pending and undergoing examination. With this amendment, claim 18 is amended and claim 23 is canceled.

Applicant reserves 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.

II. Amendments to the Specification

Paragraph [0020] on page 4 of the specification is amended to correct a typographical error. No new matter is added by way of this amendment.

III. Amendments to the Claims

Claim 18 is amended to recite wherein the ratio of emulsifier to aprepitant ranges from about 18:1 to 22:1. Support for this amendment can be found, for example, at paragraph [0018] on page 4 of the specification as filed.

Claim 18 is further amended for clarity.

Claim 23 is canceled.

No new matter is added by way of these amendments.

IV. Rejections Under 35 USC §103

Claims 18, 20-25, 27 and 31-34 are rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou et al., CN102379845A, published March 21, 2012 (hereinafter "Zhou").

Claim 26 is rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou in view of Hargreaves et al. (Annals of the New York Academy of Sciences, 2011, 1222:40-48, hereinafter "Hargreaves") and Sun et al. (Cancer Chemother. Pharmacol., 2013, 72:509-513, hereinafter "Sun").

Claims 28-30 are rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou in view of Karavas et al. (WO 2014/005606, hereinafter "Karavas"), Bromer et al. (US 2007/0071777, hereinafter "Bromer"), and Wan et al. (US 2016/0024092, hereinafter "Wan").

A. The Present Claims

The claims are directed to a method for preventing or treating a subject at risk of or suffering from emesis, comprising administering to the subject a composition comprising an injectable emulsion. The injectable emulsion aprepitant, 11 to 15 wt% of an emulsifier, an oil, a co-emulsifier which is an alcohol, a tonicity modifier, a pH modifier and water, wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1. The pH of the emulsion ranges from about 7.5 to 9.0.

B. The Cited Art

ZHOU is a published Chinese patent application. A translation of the application was provided by Applicant in the Information Disclosure Statement filed for the instant application on February 23, 2016. Zhou describes oil-in-water emulsions of aprepitant and that aprepitant can be used to treat nausea and emesis induced by chemotherapy.

SUN discusses compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids. Sun describes aprepitant as an oral formulation and does not describe emulsion formulations.

HARGREAVES reviews aprepitant as a neurokinin-1 receptor antagonist useful for managing chemotherapy-induced nausea and vomiting. Hargreaves provides a brief review of oral formulation of aprepitant and formulation of fosaprepitant for intravenous use.

KARAVAS describes injectable pharmaceutical formulations comprising aprepitant or fosaprepitant and contains a single generic reference to aqueous and non-aqueous emulsions.

BROMER describes oil-in-water emulsions of estrogen and progesterone.

WAN, the specification of which was first published as U.S. Pat. Pub. No. 2011/0038925, describes intravenous formulations, including emulsions, of an neurokinin-1 receptor antagonist. Wan does not include aprepitant as an example of a neurokinin-1 receptor antagonist.

C. The Legal Standard

An invention "composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418 (2007). "Often, it will be necessary…to look to interrelated teachings of multiple [references]….and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known element in the fashion claimed[.]" *Id.* "[T]his analysis should be made explicit," and it "can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *Id.* "We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention." *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008).

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be an apparent reason why a person of ordinary skill would have combined the prior art elements in the manner claimed. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Second, there must be a reasonable expectation of success. Third, the references when combined, must teach or suggest all the claim limitations. *Id.; Procter & Gamble Co. v. Teva Pharmaceuticals USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009); *see also M.P.E.P. § 2143.*

To sustain a *prima facie* case of obviousness, the Examiner must prevail on all three criteria. A failure on any one precludes a finding of *prima facie* obviousness. As will be articulated hereinbelow, the present rejection cannot be sustained because none of the elements has been satisfied.

According to the M.P.E.P. § 2143 I. A., the rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. *KSR*, 550 U.S. at 416, 82USPQ2d at 1395; *Sakraida v. AG Pro, Inc.*, 425U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atl. & P. Tea Co. v. Supermarket Equip.Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950)."[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to

combine the elements in the way the claimed new invention does." *KSR*, 550 U.S. at418, 82 USPQ2d at 1396. If any of these findings cannot be made, then this rationale cannot be used to support a conclusion that the claim would have been obvious to one of ordinary skill in the art.

As stated in the M.P.E.P. § 2144.09 VII, a *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties. *In re Papesch,* 315 F.2d 381, 137 USPQ43 (CCPA 1963).

The rejection is traversed for the following reasons.

D. Claims 18, 20-22, 24, 25, 27 and 31-34 are Patentable over Zhou

The present claims are directed to a method for preventing or treating a subject at risk of or suffering from emesis comprising administering to the subject an injectable emulsion which comprises aprepitant, 11 to 15 wt/wt% of an emulsifier, an oil, a co-emulsifier which is an alcohol, a tonicity modifier, a pH modifier and water, wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1. The pH of the emulsion ranges from about 7.5 to 9.0.

Zhou is cited by the Examiner as the primary reference for its teaching of the use of aprepitant as an antiemetic to treat delayed chemotherapy-induced nausea and vomiting (CINV) and for teaching an aprepitant microemulsion which comprises, e.g., 0.5 to 2.0 wt%, preferably 1.0 to 1.5 wt% aprepitant, 0.5 to 10 wt%, preferably 8 to 10 wt% emulsifier, wherein the emulsifier is egg yolk phospholipids, 5 to 30 wt%, preferably 7 to 15 wt% oil, wherein the oil is soybean oil, 1 to 10 wt%, preferably 7 to 13 wt%, alternatively preferably 2 to 5 wt% co-emulsifier, wherein the co-emulsifier is ethanol, 5 to 20 wt%, preferably 8 to 13 wt% protective agent, wherein the protective agent may be glycerin, sucrose or glucose, and 60 to 80 wt%, preferably 60-69 wt% water. The pH of the microemulsion is 6.0 to 8.0.

The Examiner asserts that while Zhou does not expressly teach a weight percent of emulsifier greater than 10 wt%, it would have been obvious to one of ordinary skill in the art at the time of invention to use 11 to 15 wt/wt% emulsifier as presently claimed. Moreover, the Examiner states that because Zhou teaches that the emulsion, containing up to 10 wt% emulsifier, may be concentrated or lyophilized prior to use, this mere dilution/concentration step, i.e., a change in size or proportion, is within the teachings of Zhou and is therefore obvious. The Examiner suggests that the difference in wt% emulsifier between Zhou and the present claims is

an obvious variant that is arrived at by routine optimization absent some demonstration of unexpected results from the claimed parameters. In response, Applicant details *inter alia* said unexpected results to show that the claims indeed are not obvious in view of Zhou.

D1. The Claimed Pharmaceutical Emulsions Possess Unexpected Results and Advantages

It is Applicant's position that the claims are patentable over Zhou in part because the composition administered to a subject according to the presently claimed method possesses unexpectedly advantageous or superior properties over any aprepitant emulsion taught or suggested by Zhou. Importantly, the stability (e.g., the lack of crystal formation) of aprepitant emulsions resulting from a formulation comprising 11 to 15 wt/wt% egg yolk lecithin (Lipoid E 80) and an emulsifier:aprepitant ratio ranging from 18:1 to 22:1 demonstrates an unexpected and unpredictable advantage of the aprepitant emulsions as recited in the present claims over the aprepitant formulations of Zhou.

The aprepitant emulsions generated as described in Examples 1, 2, 3, and 6 have emulsifier weight percentages ranging from about 11.7 to 14.3 wt/wt%, each of which falls within the claimed range of emulsifier but outside the range of emulsifier weight percentages taught by Zhou. The emulsifier:aprepitant ratio for each of Examples 1, 2, 3, and 6 is about 20:1. As shown in Table 7 on pages 27-28 of the instant specification as filed, the formulations of Examples 1, 2, 3 and 6 lacked 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. None of the emulsions described in Examples 1, 2, 3, and 6 of the instant application showed crystal formation prior to 2 or 3 months storage at room temperature.

In contrast, emulsions prepared according to Zhou are not stable, readily forming crystals in a short period of time. For example, the emulsion described in Example 4 was prepared according to compositions and methods of Zhou and comprises less than 11 wt/wt% egg yolk lecithin (9.95 wt/wt% Lipoid E 80) and an emulsifier:aprepitant ratio of about 14.8:1 (6.67 g Lipoid E 80 and 0.45 g aprepitant). Crystals were observed in the resultant emulsion within 4 days post-preparation at room temperature. Example 5 describes preparation of an aprepitant emulsion comprising 2.5 weight percent emulsifier and an emulsifier:aprepitant ratio of 10:1.

Again, crystals were observed in the emulsion within 4 days post-preparation at room temperature.

There is no basis for concluding that the present claims would have been obvious over Zhou for at least the reason that there was no motivation to modify the emulsions of Zhou. Zhou does not suggest or recognize the problem of crystal formation in aprepitant emulsions. Zhou does not suggest potential effects of emulsifier weight percent or emulsifier:aprepitant ratio on stability of an emulsion. A person having ordinary skill in the art at the time of filing could not know that the aprepitant emulsions taught by Zhou lacked stability or that modifying the emulsions of Zhou to comprise 11 wt/wt% to 15 wt/wt% emulsifier or an emulsifier:aprepitant ratio of 18:1 to 22:1. Accordingly, the claimed method is not obvious over the teachings of Zhou.

D2. Reasons to Modify the Elements of the Cited Reference Were Not Known

The obviousness rejection is based largely on the Examiner's assertion that it would have been customary for an artisan of ordinary skill to determine the optimal weight percent of emulsifier needed to achieve the desired results. There is no basis for this assertion, however, because the instant claims represent in part identification of a problem not previously recognized by Zhou. It was Applicant who showed that emulsions prepared according to the compositions and methods of Zhou form crystals no later than 4 days of storage at room temperature. In contrast, emulsions comprising 11 to 15 wt/wt% of an emulsifier wherein the ratio of emulsifier to aprepitant is within a range of about 18:1 to 22:1, as recited in the claimed method, are stable at room temperature for more than 2-3 months, forming no crystals.

As shown in Table 7 on pages 27-28 of the instant specification as filed, the formulations of Examples 1, 2, 3 and 6 lacked 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 each fall within the scope of instant claim 18.

Again, in the absence of any evidence that a person having ordinary skill in the art at the time of filing knew that the aprepitant emulsions taught by Zhou lacked stability, there is no basis for concluding that the present claims would have been obvious over Zhou because Zhou does not recognize the formation of crystals in the emulsions produced as described or the effects

of 11 to 15 weight percent emulsifier and an emulsifier:aprepitant ratio within a range of about 18:1 to 22:1 on stability of an emulsion.

To facilitate allowance of the instant application, Applicant references the prosecution history for Application Ser. No. 15/083,071 (hereinafter "the '071 application"), filed on March 28, 2016 and issued as U.S. Pat. No. 9,561,229 on February 7, 2017, which is a continuation of the instant application, and which contains claims to a pharmaceutical emulsion comprising aprepitant. During examination of the '071 application, the Examiner granted a telephonic interview with Applicant which took place on August 25, 2016 to discuss patentable distinctions of the claimed aprepitant emulsion over the Zhou publication. A summary of the interview by the Examiner is attached hereto as Exhibit A. The Examiner had requested clarification regarding preparation of the emulsions in Zhou as compared to the preparation of emulsions according to the instant specification. Specifically, the Examiner questioned whether the unexpected results (e.g., increased stability) of the emulsions claimed in the '071 application were due to a difference in the method of preparing the emulsion. Also attached herein is the Declaration by named inventor Dr. Thomas Ottoboni, filed on September 1, 2016 for the '071 application, describing the process of emulsion preparation by Zhou and comparing it to the emulsion preparation described in the instant specification. In the Declaration (attached hereto as Exhibit B), Dr. Ottoboni confirms that Example 4 describes an emulsion that was prepared according to the methods taught by Zhou, thereby supporting Applicant's assertion that the emulsion claimed in the '071 application is unexpectedly advantageous over the emulsions of Zhou.

Again, it was Applicant who recognized problems in producing aprepitant emulsions which remain stable over time. For example, as stated at paragraph [0084] bridging pages 13 to 14 of the specification as filed, aprepitant emulsions generated as described in the specification possess favorable stability properties when the amount of emulsifier in the oil phase is greater than the amount of oil. Applicant notes that the relative amounts of emulsifier and oil in the oil phase are essentially identical to the relative amounts of emulsifier and oil in the final emulsion.

Applicant herein submits that pending claim 18 as well as claims 20-23, 25, 27 and 31-34 which depend directly or indirectly from claim 18 are not obvious over Zhou for at least the reasons that the Examiner has not identified a reason that would have prompted a POSA in the relevant filed to combine elements and ranges in a way the present claims do and the claimed compositions possess unexpected and unpredictable advantages over the cited art as evidenced

by the increased stability of the claimed pharmaceutical emulsions.

E. Claim 26 is Patentable over Zhou in View of Hargreaves and Sun

Claim 26 depends from claim 18 and recites wherein the emulsion further comprises dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase. Hargreaves is relied upon for teaching that aprepitant in combination with a 5-HT3 receptor antagonist and dexamethasone can optimize protection against CINV in both acute and delayed phases. Sun is cited for teaching compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids (e.g., dexamethasone) for administration of antiemetics to patients receiving moderately or highly emetogenic chemotherapy.

Neither Hargreaves nor Sun teaches or suggests a method to treat a subject at risk of or suffering from emesis by administering a composition comprising an injectable emulsion comprising aprepitant and 11 to 15 wt/wt% of an emulsifier, wherein the emulsifier: aprepitant ratio ranges from about 18:1 to 22:1. Moreover, neither reference recognizes a problem of crystal formation in aprepitant emulsions. In the absence of this teaching or suggestion, Hargreaves and Sun fail to cure the defects of Zhou.

F. Claims 28-30 are Patentable over Zhou in View of Karavas, Bromer and Wan

Claims 28-30 are directed to various components of the emulsion as claimed in claim 18. Karavas, Bromer and Wan are cited by the Examiner for their teachings of the various components of the emulsion comprising aprepitant. Karavas describes a sterile injectable formulation containing aprepitant or fosaprepitant and is cited for teaching that the composition comprises 0.01 – 50 wt% of solubilizing or wetting agents, e.g., sodium oleate, and has a pH of about 6 to about 8, preferably about 7, which can optionally be obtained using a buffer. The Examiner cites Karavas for teaching that the pH adjusters may be acids or acid salts and may have sodium as the counterion/salt. Karavas does not teach or suggest an aprepitant emulsion comprising about 11-15 wt/wt% of an emulsifier, wherein the emulsifier:aprepitant ranges from about 18:1 to 22:1.

Bromer is directed to an oil emulsion containing estrogen and progestogen and is cited by the Examiner for teaching an emulsion comprising soybean oil, egg yolk lecithin, glycerol, water

and sodium oleate, and describing adjusting the pH of the emulsion to 6.0 to 9.0 using sodium oleate. Paragraph [0047] of Bromer states that the content of emulsifier is from 0.6 to 1.5% by weight, preferably 1.2% by weight, based on the total emulsion. Bromer does not teach or suggest an aprepitant emulsion comprising about 11-15 wt/wt% of an emulsifier, wherein the emulsifier:aprepitant ranges from about 18:1 to 22:1.

Wan is cited for teaching an intravenous formulation of neurokinin-1 antagonists and for teaching that TRIS is a suitable buffer for a pH of 7-8. Wan does not teach or suggest an aprepitant emulsion comprising about 11-15 wt/wt% of an emulsifier, wherein the emulsifier:aprepitant ranges from about 18:1 to 22:1.

In the absence of teaching by Karavas, Bromer and/or Wan of a composition comprising an injectable emulsion wherein the emulsion comprises *inter alia* aprepitant and 11 to 15 wt/wt% of an emulsifier, wherein the emulsifier:aprepitant ranges from about 18:1 to 22:1, Karavas, Bromer and Wan fail to cure the defects of Zhou.

Accordingly, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. §103.

V. Double Patenting

Claims 18 and 20-34 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of co-pending Application Serial No. 15/083,071.

Application Serial No. 15/083,071 issued on February 7, 2017 as U.S. Pat. No. 9,561,229. Applicant herein submits a Terminal Disclaimer in accordance with 37 C.F.R. § 1.321(b) and (c), thereby obviating the above obviousness type double patenting rejection over U.S. Pat. No. 9,561,229. Applicant submits that the Terminal Disclaimer overcomes the rejection for obviousness-type double patenting and withdrawal of the rejection is respectfully requested.

VI. Conclusion

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-5907 and please credit any excess fees to such deposit account. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 815-7647.

Respectfully submitted,
MCDERMOTT WILL & EMERY LLP

Date: April 18, 2017

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

Correspondence
Customer No. 108547

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McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER	
LEVIN, MIRIAM A	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
07/13/2017	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. 14/859,013	Applicant(s) OTTOBONI ET AL.	
	Examiner MIRIAM A. LEVIN	Art Unit 1613	AIA (First Inventor to File) Status Yes

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

Period for Reply

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

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

Status

1)☐ Responsive to communication(s) filed on _____.

☐ 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) *18 and 20 – 22, 24 - 34* 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) *18 and 20 – 22, 24 - 34* is/are rejected.

8)☒ Claim(s) *18* is/are objected to.

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

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

Application Papers

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

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

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

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

Priority under 35 U.S.C. § 119

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

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

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

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

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

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

Attachment(s)

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

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

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

4) ☐ Other: _____.

1. 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

2. Applicant's amendment filed April 18, 2017 has been received and entered.

Status of Claims

3. Claims Pending: 18 and 20 – 22, 24 - 34
4. New claims: None
5. Amended claims: 18
6. Canceled Claims: 1 - 17, 19, 23
7. Withdrawn claims: none
8. Change in Dependency: None

9. Elected group: III (method of treatment)
10. Elected species:
    a. Emulsifier – egg lecithin
    b. Oil = soybean oil
    c. Co-emulsifier = ethanol
    d. Tonicity modifier = sucrose
    e. pH modifier = sodium oleate
    f. buffer = TRIS

11. Objections/Rejections withdrawn: None
    g. NSDP (ODP) vs. 15/083071 – now US 9,561,229

12. Rejections maintained with revision:
    h. 35 USC 103 over Zhou (CN 102379845 A) vs. cl. 18 and 20 - 25, 27 and 31 – 34
    i. 35 USC 103 over Zhou + Hargreaves + Sun vs. cl. 26
    j. 35 USC 103 over Zhou + Karavas + Bromer + Wan vs. cl. 28 – 30

13. New Grounds and/or Rejections necessitated by amendment: None

14. Terminal Disclaimers:
    k. April 18, 2017 vs. US 9,561,229 (previously US application 15/083,071)

15. Applicant's arguments filed April 18, 2017 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Objections

16. Claim 18 is objected to because of the following informalities: please clarify the language of the claim so that it is clear that the co-emulsifier is not part of the emulsifier: aprepitant ratio. Appropriate correction is required.

Claim Rejections - 35 USC § 103

17. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

18. 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.

19. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. Claims 18 and 20 – 22, 24, 25, 27 and 31 - 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR) (cited in prior action). (Note: English translation was attached to the back of the Chinese publication. Citation is made to the English translation.)

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the

examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Applicant claims a method of treating a patient at risk of or suffering from emesis comprising administration of an injectable pharmaceutical emulsion comprising:

l. aprepitant;

m. 11 – 15 wt. % emulsifier (elected species egg yolk lecithin);

n. Oil (elected species soybean oil);

o. Co-emulsifier which is an alcohol (elected species ethanol);

p. Tonicity modifier (elected species sucrose);

q. pH modifier (elected species sodium oleate);

r. water;

s. wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1, and

t. wherein the emulsion has a pH of 7.5 – 9.0.

Determination of the scope and content of the prior art (MPEP 2141.01)

23. Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. (title)

24. Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003]) CINV is chemotherapy-induced nausea and vomiting.

25. The emulsion comprises, for example:

u. 0.5 - 2.0 wt. % aprepitant, preferably 1.0 - 1.5 wt. %;

v. 0.5 – 10 wt. % emulsifier; preferably 8 – 10 wt. %, wherein the emulsifier is egg yolk phospholipids;

w. 5 – 30 wt. % oil, preferably 7 – 15 wt. % oil, wherein the oil is soybean oil;

x. 1 – 10 wt. % co-emulsifier, preferably 7 – 13 wt. % co-emulsifier; alternatively, preferably 2 – 5 wt. %, wherein the co-emulsifier is ethanol;

y. 5 – 20 wt. % of a protective agent (compare vs. tonicity modifier of instant claims), preferably 8 – 13 wt. %, wherein the protective agent may be glycerin, sucrose or glucose;

z. 60 – 80 wt. % water, preferably 60 – 69 wt. %;

aa. Wherein the pH of the microemulsion is 6.0 - 8.0.

bb. (See, e.g. cl. 1, 5 – 9; [0008] – [0011]; see also examples).

26. Therefore, Zhou et al. teach or suggest an emulsifier: aprepitant ratio of 20:1 to 1:4, i.e., 10:0.5 to 0.5 to 2.0, based on weight percentages recited above. Zhou et al. examples 1 - 6 and 8 with ratios of 1:1 to 13:1 emulsifier: aprepitant. (Ex. 1 - 6, 8)

27. In Ex. 7, Zhou et al. teach 0.2 g aprepitant and 9.8 g of egg yolk phospholipid. ([0032]) First, 0.2 g wt. % of aprepitant is outside the range recited earlier in the document and second, this example provides a 49:1 ratio of emulsifier to aprepitant. **Therefore, Zhou et al. teach that there is some flexibility in the ranges recited earlier in the document.**

28. In regard to the pH, in examples using the egg yolk phospholipid, Zhou et al. teach pHs of 6.8, 7.2 and 8.0. (Ex. 1, 4 – 7)

29. Zhou et al. teach the emulsion may then be lyophilized for later use. (e.g. [0026])

30. Zhou et al. teach that the emulsion may be concentrated into small-volume injection vials. For example, in Ex. 5, 115 mg aprepitant emulsion is placed in a 5 mL vial. The starting emulsion has 2 grams of aprepitant. 2 grams / 0.115 grams = 17.39 aliquots. If each aliquot is 5 mL, that only accounts for 86 mL, which is probably not the entire volume. (See, [0028])

31. In Ex. 6, the emulsion comprises 0.5 g aprepitant, and each 5 mL aliquot comprises 150 mg; or nearly 1/3 of the total. (See, e.g. [0029], [0030]) Clearly this emulsion must have been concentrated prior to being placed in the 5 mL vial.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

32. The difference between the instant application and Zhou et al. is that Zhou et al. do not expressly teach a weight percent of emulsifier greater than 10 wt. %.

Finding of prima facie obviousness Rationale and Motivation (MPEP 2142-2143)

33. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use 11 – 15 wt. % emulsifier, and a ratio of 18:1 to 22:1, as suggested by Zhou et al., and produce the instant invention.

34. One of ordinary skill in the art would have been motivated to do this because these ranges lie within, border on, or are close to, the ranges taught and/or suggested by Zhou et al.

35. Zhou et al. teach 0.5 to 10 wt. % emulsifier, preferably 8 – 10 wt.%, and 0.5 - 2.0 wt. % aprepitant, which provides the teaching, suggestion and /or motivation for a ratio of emulsifier to aprepitant of 20:1 to 1:4, preferably 20:1 to 4:1. Zhou et al. also teach an example using 10 wt. % egg yolk phospholipids and 0.2 wt. % aprepitant, which is an emulsifier: aprepitant ratio of 49:1, thereby teaching that there is flexibility in regard to the ranges recited earlier in the document, i.e. the ranges should be interpreted as preferred or most preferred, but not limiting.

36. With the exception of the emulsifier, the weight percentage of every ingredient, ratio of emulsifier to aprepitant, and pH of the emulsion lie within, overlap or border on the ranges explicitly taught by Zhou et al. The instantly claimed wt. % range of the emulsifier is only slightly above that of Zhou et al. (11 vs. 10) and Ex. 7 of Zhou et al. teaches that the ranges are not limiting, therefore slight variations are within the teachings of Zhou.

37. Therefore the claimed ranges are obvious for one or more of the following reasons:

cc. The range is anticipated. (MPEP 2131.03 (I)(A))

dd. The range is obvious (MPEP 2144.05 (I) Overlap of ranges) – including ranges which do not overlap but are close

ee. Changes in concentration are routine optimization (MPEP 2144.05 (II)(A))

2131.03Anticipation of Ranges [R-6]

I. A SPECIFIC EXAMPLE IN THE PRIOR ART WHICH IS WITHIN A CLAIMED RANGE ANTICIPATES THE RANGE

"[W]hen, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art." *Titanium Metals Corp. v. Banner,* 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (citing *In re Petering*, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)) (emphasis in original)

2144.05 Obviousness of Ranges [R-5]

I. OVERLAP OF RANGES

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, 191USPQ 90 (CCPA 1976) . . . Similarly, 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) . . .

2144.05 Obviousness of Ranges [R-5]

II. OPTIMIZATION OF RANGES

A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[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 (CCPA1955)

38. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal wt. % of emulsifier needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of the wt. % of emulsifier would have been obvious at the time of Applicant's invention.

39. In regard to prevention or treatment of emesis, e.g. induced by chemotherapy, Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003]) (NOTE: CINV is chemotherapy-induced nausea and vomiting.)

40. In regard to the aprepitant being present in the oil phase (instant cl. 23), because the compositions are comprised of the same compounds, the composition will have the same chemical and physical properties.

"A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

41. Claims 18 and 20 – 22, 24, 25, 27 and 31 - 34 are rejected.

42. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

43. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Zhou + Hargreaves + Sun

44. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR), in view of Hargreaves et al. (Development of aprepitant, the first neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting, Annals of the New York Academy of Sciences (Ann. N.Y. Acad. Sci.) (2011) 1222: 40-48 (Issue: Pharmaceutical Science to Improve the Human Condition: Prix Galien, 2010), and Sun et al. (Compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids, Cancer Chemother. Pharmacol. (2013) (available on-line July 17, 2013) 72: 509 - 513).

Determination of the scope and content of the prior art (MPEP 2141.01)

45. As discussed above, Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. Zhou et al. teach aprepitant is used as an antiemetic to treat delayed CINV. (e.g. [0002], [0003])

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

46. The difference between the instant application and Zhou et al. is that Zhou et al. do not expressly teach the composition further comprising dexamethasone sodium phosphate. This deficiency in Zhou et al. is cured by the teachings of Hargreaves et al. and Sun et al.

47. Hargreaves et al. teach development of aprepitant, the first neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting (CINV) where "[a]prepitant, in combination with a 5-HT3 receptor antagonist and dexamethasone, optimizes protection against CINV in both the acute and delayed phases compared to the prior standard of care, and is now recommended as the first-

line therapy for patients about to be treated with moderately or high emetogenic chemotherapy." (title, abstract, conclusion)

48. Sun et al. teach "Compatibility of intravenous fosaprepitant with intravenous 5-HT3 antagonists and corticosteroids," wherein dexamethasone sodium phosphate is one of two corticosteroids tested, "Fosaprepitant demonstrated compatibility when combined in the same IV infusion bag with common 5-HT3 antagonists and corticosteroids for storage and IV administration . . ." and "[u]se of fosaprepitant in combination with other antiemetics may provide a flexible option for administration of antiemetics to patients receiving moderately or highly emetogenic chemotherapy."(Title, Abs.)

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

49. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use dexamethasone sodium phosphate in the aprepitant composition to treat CINV, as suggested by Zhou et al., Hargreaves et al., and Sun et al., and produce the instant invention.

50. One of ordinary skill in the art would have been motivated to do this because all three references teach aprepitant to treat CINV (chemotherapy induced nausea and vomiting), Hargreaves et al. teach aprepitant plus dexamethasone and a 5-HT3 antagonist as first-line therapy for CINV, and Sun et al. teach dexamethasone sodium phosphate as a form of the drug that is compatible with aprepitant for IV administration. The combination of references provide strong motivation to use the two drugs in combination to treat CINV, and to use the sodium phosphate salt as a preferred form of dexamethasone.

51. Claim 26 is rejected.

52. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

53. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Zhou + Karavas + Bromer + Wan

54. Claims 28 - 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Zhou et al. (CN 102379845 A; published March 21, 2012; cited on IDS and ISR) (cited above), in view of Karavas et al. (WO 2014/005606 A1; cited on IDS and ISR), Bromer et al. (US 2007/0071777 A1; cited on IDS) and Wan et al. (US 2016/0024092 A1; cited on IDS and ISR).

Determination of the scope and content of the prior art (MPEP 2141.01)

55. As discussed above, Zhou et al. teach aprepitant microemulsion for injection and preparation method thereof. (title) The emulsion comprises, for example:

ff. 0.5 - 2.0 wt. % aprepitant, preferably 1.0 - 1.5 wt. %;

gg. 5 – 30 wt. % oil, preferably 7 – 15 wt. % oil, wherein the oil is soybean oil;

hh. 0.5 – 10 wt. % emulsifier; preferably 8 – 10 wt. %, wherein the emulsifier is egg yolk phospholipids;

ii. 1 – 10 wt. % co-emulsifier, preferably 2 – 5 wt. %, wherein the co-emulsifier is ethanol;

jj. 5 – 20 wt. % of a protective agent, preferably 8 – 13 wt. %, wherein the protective agent may be glycerin, sucrose or glucose;

kk. 60 – 80 wt. % water, preferably 60 – 69 wt. %;

ll. Wherein the pH of the microemulsion is 6.0 - 8.0.

mm. (See, e.g. cl. 1, 5 – 9; [0008] – [0011]; see also examples).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

56. The difference between the instant application and Zhou et al. is that while Zhou et al. teach emulsifiers and a desired pH, Zhou et al. do not expressly teach sodium oleate or buffers, such as TRIS. These deficiencies in Zhou et al. are cured by the teachings of Karavas et al., Bromer et al. and Wan et al.

57. Karavas et al. teach stable injectable pharmaceutical compositions of neurokinin 1 receptor antagonist and process for preparation thereof. (Title) The neurokinin 1 receptor antagonist is preferable Aprepitant. (Abs.) The composition comprises 0.01 - 50 wt. % of solubilizing or wetting agents, such as sodium oleate (e.g., p. 4, l. 41 - p. 5, l. 8; p. 6, l. 48 - p. 7, l. 8; p. 9, ll. 28- 37; cl. 9,). The composition has

a pH of about 6 to about 8, preferably about 7, which can optionally be obtained using a buffer; the pH adjusters may be acids or acid salts and may have sodium as the counterion / salt. (e.g. p. 5, ll. 19 - 25; p. 6, ll. 41 - 46; p. 7, ll. 30 – 38; p. 9, ll. 20 – 21; p. 9, ll. 39 – 47; cl. 9).

58. Bromer et al. teach an oil emulsion for postnatal hormone substitution (title). The composition may be administered intravenously and may be administered to premature babies. (abs.) An example of the composition comprises soybean oil, egg yolk lecithin (phospholipids), glycerol, water, and sodium oleate. (e.g. [0059], Table 1; see also, e.g., [0037], [0047], [0058]). The pH is adjusted to 6.0 to 9.0 and sodium oleate may be used to adjust the pH of the oil in water emulsion. (e.g. [0053], [0058])

59. Wan et al. teach intravenous formulations of neurokinin-1 antagonists. (Title) Wan et al. teach that TRIS is a suitable buffer for a pH of 7 - 8. (e.g. [0130])

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

60. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use sodium oleate or TRIS buffer in the composition, as suggested by Zhou et al., Bromer et al., and Wan et al., and produce the instant invention.

61. One of ordinary skill in the art would have been motivated to do this because Zhou et al. teach a desired pH of 6 – 8, but do not recite any particular agent as preferred for adjusting the pH, therefore any suitable compounds may be used. Karavas et al. teach that sodium oleate and buffers may be used in injectable formulations of aprepitant. Bromer et al. teach that sodium oleate may be used a pH adjuster to obtain a pH of 6 - 9, and Wan et al. teach that TRIS may be used to obtain a pH of 7 - 8.

62. In the absence of unexpected results or other evidence to the contrary, the selection of sodium oleate or TRIS buffer is the mere selection of a material suitable for the intended use. (MPEP 2144.07)

63. As a second motivation, it is well known in chemistry that use of buffer solutions can provide a more stable or resilient pH. Buffer solutions are formed by using both acid and base, or the salt of an acid. Sodium oleate is the acid salt of oleic acid and sodium hydroxide. Soybean oil contains oleic acid, therefore by using sodium oleate to adjust the pH of the composition, a buffered solution (emulsion) is

obtained. This provides additional motivation for the selection of sodium oleate, and assurance of predictable results.

64. TRIS buffer is already a buffer solution; therefore it also provides the more stable pH obtained with a buffered solution.

65. As further motivation in regard to the selection of sodium oleate, and assurance of predictable results / reasonable expectation of success: the composition of Bromer is an oil-in-water emulsion, as is the one of Zhou. Both comprise soybean oil and egg yolk lecithin and both compositions may be injected; the composition of Bromer may be injected in infants. Because both compositions are oil-in-water emulsions, both use similar aqueous phases (glycerol and water), oil phases (soybean oil) and emulsifiers (egg yolk lecithin); and both are intended for use as injectable compositions, use of the same pH adjuster (sodium oleate) is an obvious option and, because of the similarity in the compositions, there is a reasonable expectation of success.

66. The following motivations apply:

2141>Examination Guidelines for Determining Obviousness Under < 35 U.S.C. 103 [R-6]**

III. RATIONALES TO SUPPORT REJECTIONS UNDER 35 U.S.C. 103

(A)Combining prior art elements according to known methods to yield predictable results;
(B)Simple substitution of one known element for another to obtain predictable results;
(E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
(G)Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

67. Claims 28 – 30 are rejected.

68. In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

69. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

70.

Response to Arguments

1. Applicant's arguments filed April 18, 2017 ("Remarks"), including Exhibits A - C, (note Exhibit B is the Declaration of Dr. Ottoboni (Dec.)), have been fully considered but they are not persuasive. Applicant argues unexpected results /criticality of the range, pointing to, e.g. Table 7 on pages 27 and 28 of the instant specification and comparing examples of their invention (ex. 1, 2, 3, 6) to those allegedly of Zhou et al. (e.g., Ex. 4, 5) and observing that the examples representative of their invention are stable, i.e., do not crystallize out prior to 2 – 3 months of storage, while those allegedly of Zhou showed crystals within 4 days. (Remarks, pp. 9, 10) The Examiner respectfully disagrees.

2. While the data suggests potential unexpected results or criticality of the range, there are issues which need to be addressed.

3. The first issue is that of pH. Zhou et al. teach a pH of 6 - 8 and, in the examples using the egg yolk phospholipid, adjust the pH to 6.8, 7.2 or 8.0 (Ex. 1 and 4 -7) The allegedly comparative examples in the instant specification recite a pH of "less than 8" (Ex. 4, p. 24) or do not disclose any pH at all (Ex. 5, p. 25), nor does Dr. Ottoboni directly address this issue in the Dec. Therefore because the pHs of the respective solutions are not disclosed, it is impossible to determine if the compositions are comparable in that respect. This leaves open the possibility that the crystallization is due to a difference in pH, particularly if the pH is below the range taught by Zhou et al.

4. The second issue is one of criticality of the range. Typically to demonstrate this, one would need to provide a side-by-side comparison where the ONLY variable is the ratio which is alleged to be critical and which shows that above and below the claimed range one does not see the alleged unexpected result. Applicant has not provided data of this nature.

5. Therefore the allegation of unexpected results / criticality of the range is not persuasive.

6. Applicant argues there is no motivation / insufficient motivation to optimize the weight percentages because Zhou et al. did not recognize the stability problem identified by Applicant. (Remarks, pp. 10 - 12) Applicant also provides information regarding the determination of allowability of a copending application and asserts that this should facilitate allowance of the instant claims. (Remarks, p. 11) The Examiner respectfully disagrees.

7. While it is true that Zhou et al. do not indicate the crystallization problem, neither have Applicants demonstrated that it was a problem for Zhou et al. because it is not clear that the pH of the comparative examples is the same as the pH used by Zhou.

8. Moreover, while the Examples of a reference are useful as guidance, they do not fully define the prior art invention. The ranges of Zhou et al. anticipate, encompass, overlap or border on almost every limitation of the instant claims and the only range that differs, i.e. the weight % of emulsifier, is so close that Applicant must demonstrate that the compositions are materially different, i.e. must demonstrate criticality of the claimed range by showing a side-by-side comparison where the only variable is the wt. % of emulsifier.

9. In regard to the copending case that was allowed, while the analysis used in that case is helpful, it is not persuasive. The Examiner believes that further evidence and/or amendment is needed before the instant claims can be allowed.

10. These arguments are not persuasive.

11. In regard to claims 26 and 28 - 30, the core issue is the same as for claim 18 and the other claims covered by the rejection over Zhou (Remarks, pp. 12, 13), therefore these arguments have been addressed.

12. In regard to the double patenting rejection, the terminal disclaimer was approved and therefore this rejection is overcome. (Remarks, p. 13) Therefore this rejection is withdrawn.

13. All of the arguments have been considered. The rejections under 35 USC 103 are revised and maintained; the double patenting rejection is withdrawn.

Conclusion

Claims 18, 20 – 22 and 24 - 34 are rejected. No claims are allowed.

71. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date

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

Any inquiry regarding this communication or earlier communications from the examiner should be directed to Miriam Levin whose telephone number is 571-270-3471. The examiner can normally be reached between the hours of 10:00 AM - 6:30 PM, EST, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon can be reached at 571-272-0581. The fax number for the organization where this application or proceeding is assigned is 571-273-4371.

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 any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/M. A. L./

Examiner, Art Unit 1613

/ERNST V ARNOLD/

Primary Examiner, Art Unit 1613

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/859,013	09/18/2015	Thomas B. Ottoboni	092459-0170/8027.US00	7185

108547 7590 08/22/2017

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER	
LEVIN, MIRIAM A	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
08/22/2017	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

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	14/859,013	OTTOBONI ET AL.	
	Examiner	Art Unit	
	MIRIAM A. LEVIN	1613	

All participants (applicant, applicant's representative, PTO personnel):

(1) *MIRIAM A. LEVIN*. (3)_____.

(2) *Wen Li*. (4)_____.

Date of Interview: *17 August 2017*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *18*.

Identification of prior art discussed: _____.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/ERNST V ARNOLD/
Primary Examiner, Art Unit 1613

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Ms. Li contacted the Examiner on August 8, 2017 regarding potential claim amendments that might make the instant claims allowable. Ms. Li noted that related applcation 15/083071 was previously allowed and had issued as US 9,561,229.

The Examiner advised that she would confer with her primary and would call back.

Ms. Li aslo inquired about when the Examiner thought she might be able to start work on copending application 15/398928. The Examiner advised it would probably be about 4 - 6 months, but might be longer if more RCEs were docketd to her.

After consultation with Primary Examiner Ernst Arnold, the Examiner called on 8/17/2017 to propose the following claim amendment:

In claim 18, line 3, after the word "injectable" please insert the words "physically stable." This is supported by [0068] of the specification and by the assertion of unexpected results (see, e.g. Remarks filed 4/18/2017, pp. 9, 10).

Ms. Li will confer with her client and will probably file a response with amended claims. .

REPLY UNDER 37 C.F.R. § 1.116 – EXPEDITED PROCEDURE
TECHNOLOGY CENTER 1600

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Thomas B. Ottoboni et al.	Examiner:	Miriam A. Levin
Application No.:	14/859,013	Art Unit:	1613
Filed:	September 18, 2015	Conf. No:	7185
For:	**EMULSION FORMULATIONS OF APREPITANT**		

AMENDMENT 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 responds to the final Office action dated July 13, 2017 in the above-referenced patent application.

Amendments to the Claims begin on page 2.

Remarks begin on page 5.

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.-17. (Canceled)

18. (Currently amended) A method for preventing or treating a subject at risk of or suffering from emesis, comprising administering to the subject a composition comprising an injectable physical stable emulsion wherein the emulsion comprises:

aprepitant;

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

an oil;

a co-emulsifier which is an alcohol;

a tonicity modifier;

a pH modifier; and

water;

wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1, and

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

19. (Canceled)

20. (Previously presented) The method according to claim 18, wherein the emesis is induced by chemotherapy.

21. (Previously presented) The method according to claim 18, wherein the emesis is induced by highly emetogenic chemotherapy.

22. (Previously presented) The method according to claim 18, wherein the ratio of the oil to the aprepitant within the oil phase of the emulsion ranges from about 10:1 to 15:1 (wt/wt%).

23. (Canceled)

24. (Currently Amended) The method according to claim 18, wherein the ratio of the emulsifier to the oil ranges from about 1:1 to 3:1 (wt/wt%).

25. (Previously presented) The method according to claim 24, wherein the emulsifier in the emulsion is a phospholipid.

26. (Previously presented) The method according to claim 18, wherein the emulsion further comprises dexamethasone sodium phosphate, wherein the dexamethasone sodium phosphate is present in the aqueous phase.

27. (Previously presented) The method according to claim 18, wherein the emulsifier in the emulsion is an egg lecithin.

28. (Previously presented) The method according to claim 18, wherein the pH modifier in the emulsion is sodium oleate.

29. (Previously presented) The method according to claim 18, wherein the emulsion further comprises a buffer.

30. (Previously presented) The method according to claim 29, wherein the buffer is Tris buffer.

31. (Previously presented) The method according to claim 18, wherein the oil in the emulsion is soybean oil.

32. (Previously presented) The method according to claim 18, wherein the alcohol in the emulsion is ethanol.

33. (Previously presented) The method according to claim 32, wherein the ethanol is present in the emulsion at less than 10 wt/wt%.

34. (Previously presented) The method according to claim 32, wherein the tonicity modifier in the emulsion is sucrose.

REMARKS

Consideration of the remarks presented herein is respectfully requested.

I. Status of the Claims

Claims 1-17, 19, and 23 were previously cancelled without prejudice or disclaimer.

Claims 18 and 20-34 are pending and undergoing examination. With this amendment, claim 18 is amended to insert "physically stable" after the word "injection". Support for the amendment can be found in the application as filed, for example, at ¶[0068].

Claim 24 is formally amended to make the subject matter more clear.

Therefore, there is no issue of new matter.

Applicant reserves 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.

II. Interview Summary

Applicant would like to thank Examiner Levin for the courtesies extended to the undersigned in the telephonic interview held on August 17, 2017. The undersigned contacted Examiner Levin on August 8, 2017 to discuss potential amendments, indicating that a related application 15/083,071 issued as US 9,561,229. Examiner Levin advised that she would discuss with her primary examiner and call back to suggest claim amendments. Examiner Levin contacted the undersigned on August 17, 2017, proposing to amend claim 18 to insert "physically stable" after the word "injection". The undersigned indicated that claim 18 would be amended accordingly upon Applicant's approval.

Per the undersigned's inquiry on August 8, 2017, Examiner Levin also advised the time when she would take up the copending application 15/398,928, which would probably be about 4-6 months and could be longer if more RCEs appeared on her docket.

III. Claims Objections

Claim 18 is objected to because, according to the Examiner, it is unclear whether the co-emulsifier is part of the emulsifier:aprepitant ratio. Office Action at p.2. Applicant respectfully disagrees. A skilled artisan would understand from the specification that the emulsifier and co-emulsifier are two entities. *See*, for example, specification as filed at ¶0087]. Accordingly, co-emulsifier is not part of the emulsifier:aprepitant ratio. Applicant respectfully requests that the objection be withdrawn.

IV. Rejections Under 35 USC §103

Claims 18, 20-22, 24, 25, 27 and 31-34 are rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou et al., CN102379845A, published March 21, 2012 (hereinafter "Zhou"). Office Action at pp. 3-8

Claim 26 is rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou in view of Hargreaves et al. (Annals of the New York Academy of Sciences, 2011, 1222:40-48, hereinafter "Hargreaves") and Sun et al. (Cancer Chemother. Pharmacol., 2013, 72:509-513, hereinafter "Sun"). Id. at pp. 8-9.

Claims 28-30 are rejected under 35 U.S.C. §103 as allegedly unpatentable (i.e., obvious) over Zhou in view of Karavas et al. (WO 2014/005606, hereinafter "Karavas"), Bromer et al. (US 2007/0071777, hereinafter "Bromer"), and Wan et al. (US 2016/0024092, hereinafter "Wan"). Id. at pp.10-12.

Applicant respectfully disagrees with the rejection for reasons submitted on April 18, 2017. Moreover, solely to advance prosecution, Applicant has amended claim 18 in accordance with the Office's suggestions (See Applicant-Initiated Interview Summary mailed August 22, 2017). Applicant believes that this response has fully addressed the remaining rejections.

Accordingly, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. §103.

V. Conclusion

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 50-5907 and please credit any excess fees to such deposit account. If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 815-7399.

Respectfully submitted,
MCDERMOTT WILL & EMERY LLP

Date: September 1, 2017

/Wen Li/
Wen Li
Reg. No. 62,185

Correspondence
Customer No. 108547

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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NOTICE OF ALLOWANCE AND FEE(S) DUE

108547 7590 09/18/2017
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER
LEVIN, MIRIAM A

ART UNIT	PAPER NUMBER
1613	

DATE MAILED: 09/18/2017

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/859,013	09/18/2015	Thomas B. Ottoboni	092459-0170/8027.US00	7185

TITLE OF INVENTION: EMULSION FORMULATIONS OF APREPITANT

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	12/18/2017

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 09/18/2017
McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 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)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/859,013	09/18/2015	Thomas B. Ottoboni	092459-0170/8027.US00	7185

TITLE OF INVENTION: EMULSION FORMULATIONS OF APREPITANT

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	12/18/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEVIN, MIRIAM A	1613	424-400000

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 — 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.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

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108547 7590 09/18/2017

McDermott Will & Emery LLP
500 North Capitol Street NW
Washington, DC 20001

EXAMINER	
LEVIN, MIRIAM A	

ART UNIT	PAPER NUMBER
1613	

DATE MAILED: 09/18/2017

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 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. 14/859,013	Applicant(s) Ottoboni et al.	
	Examiner MIRIAM A LEVIN	Art Unit 1613	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 Amendment after final filed Sept. 1, 2017 .
   ☐ 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 See Continuation Sheet . 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 See Continuation Sheet .

/ERNST V ARNOLD/
Primary Examiner, Art Unit 1613

Continuation of 3. The allowed claim(s) is/are: 18, 20 – 22 and 24 - 34

Continuation of Attachment(s) 7. Other: Search history, Issue Classification, Search Notes, Index of Claims, Interview Summary, BIB

Notice of Pre-AIA or AIA Status

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

DETAILED ACTION

2. Applicant's amendment filed September 1, 2017 has been received and entered.

Status of Claims

3. Claims Pending: 18 and 20 – 22, 24 - 34
4. New claims: None
5. Amended claims: 18
6. Canceled Claims: 1 - 17, 19, 23
7. Withdrawn claims: none
8. Change in Dependency: None

9. Elected group: III (method of treatment)
10. Elected species:
    a. Emulsifier – egg lecithin
    b. Oil = soybean oil
    c. Co-emulsifier = ethanol
    d. Tonicity modifier = sucrose
    e. pH modifier = sodium oleate
    f. buffer = TRIS

11. Objections/Rejections withdrawn: None
    g. Objection to cl. 18
    h. 35 USC 103 over Zhou (CN 102379845 A) vs. cl. 18, 20 - 25, 27, 31 – 34
    i. 35 USC 103 over Zhou + Hargreaves + Sun vs. cl. 26
    j. 35 USC 103 over Zhou + Karavas + Bromer + Wan vs. cl. 28 – 30

12. Rejections maintained with revision: None

13. New Grounds and/or Rejections necessitated by amendment: None

14. Terminal Disclaimers:
    k. April 18, 2017 vs. US 9,561,229 (previously US application 15/083,071)

15. Applicant's arguments filed September 1, 2017 have been fully considered. There are no rejections or objections applied against the instant claims.

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 an interview with Wen Li on September 8, 2017.

The application has been amended as follows; the only amendment is to claim 18, therefore it is the only claim recited below:

> 18. (Currently amended) A method for preventing or treating a subject at risk of or suffering from emesis, comprising administering to the subject a composition comprising an injectable physically stable emulsion wherein the emulsion comprises:
>
> aprepitant;
>
> 11 wt/wt% to 15 wt/wt% of an emulsifier; an oil;
>
> a co-emulsifier which is an alcohol; a tonicity modifier; a pH modifier; and water;
>
> wherein the ratio of emulsifier:aprepitant ranges from about 18:1 to 22:1, and wherein the pH of the emulsion ranges from about 7.5 to 9.0.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: Per the Examiner's discussion with Primary Examiner Ernst Arnold, and the Interview summary, Applicant has demonstrated unexpected results in regard to physical stability of the

instantly claimed composition. The claims have now been amended to reflect this property and are therefore allowable.

Discussion of the closest prior art may be found in the prior office actions, and in the response to arguments below.

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."

Response to Arguments

1. Applicant's arguments filed September 1, 2017 ("Remarks"), with respect to the objections and rejections of the claims, have been fully considered and are persuasive. Therefore the objections and rejections have been withdrawn.

2. In regard to the objection to claim 18, Applicant argues that it is clear from the specification, e.g. [0087] of spec as filed, that the emulsifier and co-emulsifier and treated as two separate entities. (Remarks, p. 5) The Examiner agrees. The objection is withdrawn.

3. In regard to the rejections under 35 USC 103, Applicant re-asserts the arguments of April 18, 2017 (Remarks, p. 5), which include assertions of unexpected results in regard to the stability of the instantly claimed composition. (Remarks of April 18, 2017; Dec. of Dr. Ottoboni and Exhibits A – C; see also Response to Arguments section of Final Rejection of July 13, 2017.) Upon further consideration and consultation with Primary Examiner Ernst Arnold, the Examiner accepts that Applicant has demonstrated

unexpected results in regard to the physical stability of the composition when compared to compositions of the prior art. The claims have been amended accordingly and are therefore now allowable.

4. All of the arguments have been considered. The arguments are persuasive, therefore the Objections and Rejections are withdrawn.

Conclusion

Claims 18, 20 – 22 and 24 - 34 are allowed. No claims are rejected.

Any inquiry regarding this communication or earlier communications from the examiner should be directed to Miriam Levin whose telephone number is 571-270-3471. The examiner can normally be reached between the hours of 10:00 AM - 6:30 PM, EST, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon can be reached at 571-272-0581. The fax number for the organization where this application or proceeding is assigned is 571-273-4371.

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 any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/M. A. L./

Examiner, Art Unit 1613

/ERNST V ARNOLD/
Primary Examiner, Art Unit 1613