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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/855,168	09/15/2015	Stephen Ruddy	SHR-1204US	8760
139375 7590 07/12/2016 Shire Human Genetics Therapies, Inc. c/o Proskauer Rose LLP One International Place Boston, MA 02110			EXAMINER MIKNIS, ZACHARY J	
			ART UNIT 1675	PAPER NUMBER
			NOTIFICATION DATE 07/12/2016	DELIVERY MODE ELECTRONIC

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

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

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

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<b>Office Action Summary</b>	<b>Application No.</b> 14/855,168	<b>Applicant(s)</b> RUDDY ET AL.	
	<b>Examiner</b> ZACHARY J. MIKNIS	<b>Art Unit</b> 1675	<b>AIA (First Inventor to File) Status</b> No

**-- 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 23 November 2015.  
☐ 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) 16,18,20,21,32-35 and 46-53 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) 16,18,20,21,32-35 and 46-53 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](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

**Application Papers**

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☒ The drawing(s) filed on 23 March 2016 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) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                               | 3) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) | Paper No(s)/Mail Date. ____.                            |
| Paper No(s)/Mail Date ____.   | 4) <input type="checkbox"/> Other: ____.                |

## **DETAILED ACTION**

### ***Notice of Pre-AIA or AIA Status***

The present application is being examined under the pre-AIA first to invent provisions.

### ***Claim Status***

Claims 1-15, 17, 19, 22-31 and 36-45 have been canceled. Claims 16, 18, 20, 21, 32-35, and 46-53 are pending and are being examined on the merits.

### ***Election/Restrictions***

Applicant's election without traverse of Group I (claims 16-35) in the reply filed on 23 November 2015 is acknowledged.

Claims 36-45 (drawn to Group II) have been canceled by the Applicant prior to allowance. Per MPEP 821.04(b), the restriction is maintained and made FINAL in order to preserve Applicant's rights under 35 U.S.C. 121 with respect to double patenting.

### ***Declarations Under 37 C.F.R. 1.132***

1. The Declaration of Michael Frank is found to be sufficient to establish that the Jiang art is not anticipatory, demonstrating that it featured administration of Cinryze at 100 U/mL, not the at least 400 U/mL as now claimed. Additionally, the Frank

Declaration establishes the total volume of the injection (8 to 11.5 mL) and timing (30 to 60 minutes).

2. The Declaration of Jennifer Schranz has been considered and found partially persuasive. The Schranz Declaration is found to establish that the Kreuz art utilized a dosage of 50 U/mL over a larger 10 mL volume and for 15 minutes. The Schranz declaration establishes that Anonymous required hyaluronidase for delivery and was at a dose below that being claimed and at a far higher volume than normally found for subcutaneous delivery.

**I. New Rejections:**

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 16, 18, 20, 21, 32-35, 46, 47, and 49-52** are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over **Jiang** et al. (Clinical Immunology 136:323-328, published 8 June 2010, hereafter referred to as Jiang) and **Anonymous** (The Pharmaceutics and Compounding Laboratory: Subcutaneous at <http://pharmlabs.unc.edu/labs/parenterals/subcutaneous.htm>, published 14 June 2010, hereafter referred to as **UNC**).

The Jiang art teaches that Cinryze is approved by the FDA for intravenous administration for prophylactic use in patients with HAE (see e.g. p.323 Col.2 ¶1). It is also taught that HAE patients can have a prodrome period of 1-2 hours, during which

administration of C1 inhibitor can be given to treat acute attacks of HAE (see e.g. p.323 Col.2 ¶2 to p.324 Col.1 ¶1). The Jiang art teaches that Cinryze was administered to 16-23 kg pigs at a dosage of 50 U/kg (i.e. 800 to 1150 U in total) intravenously or subcutaneously (see e.g. Materials and Methods, *In vivo* study design). Infusions given subcutaneously were administered on days 0, 3, and 6 (see e.g. p.325 Col.1 ¶1). The IV infusions of Cinryze peaked at 1 hr post-infusion and gradually declined over 3 days, while for subcutaneous administration peak levels were achieved at 6 hrs and were stable over the next three days (see e.g. *In vivo* protein levels). The Jiang art concludes that subcutaneous administration is a viable treatment option for patients with HAE (see e.g. p.328 Col.1 ¶4).

The difference between Jiang and the claimed invention is that Jiang does not teach treatment of patients in need thereof in a specific embodiment, but is fairly suggestive of the claimed method. Additionally, Jiang does not teach the dosage of about 400 U/mL in a single subcutaneous dose.

With respect to the dosage of 400 U/ml, one of skill in the art would recognize that a subcutaneous dose of any drug is limited generally to a total injection volume of approximately 2 mL. For instance, see e.g. the previously cited art from UNC. The administered dosage of Cinryze is already known to be 1000 U (for instance, see e.g. FDA Clinical Pharmacology Review from 4 December 2007, in particular p.2), and in transfer of drugs from IV administration to subcutaneous administration it is generally still sought to deliver the same dosage. Logically, the conversion of a dose utilized for I.V. administration to the equivalent total dose for subcutaneous administration would

require the compound itself to be more concentrated, owing to the lower volume of the subcutaneous dose. Other anti-HAE drugs are known for subcutaneous administration (for instance Ecallantide, a 60 amino acid-long peptide) which would provide motivation for other HAE drugs such as Cinryze to be administered subcutaneously, especially given that Cinryze is also a long peptide.

It would be obvious to one of ordinary skill in the art at the time of invention that the subcutaneous administration of Cinryze to pigs as taught in Jiang could also be applied to human patients suffering from HAE, given that Jiang teaches that Cinryze is already administered to said patients to treat HAE, albeit intravenously. The teachings of volume limitations of subcutaneous doses would limit the 1000 U of Cinryze to a 2 mL subcutaneous dose, which would have at least 400 U/mL, even considering that Jiang used doses of 100 U/mL (i.e. the artisan would have a motivation from the prior art to make the injection of the entire Cinryze dose limited to a 2 mL volume, resulting in at least 400 U/mL). The resulting increase in blood level would be expected to inherently occur, as the prior art provides for the same method of administration and total volume. The good pharmacokinetics of Cinryze from subcutaneous administration and stable blood profile as compared to IV-administered Cinryze as found in Jiang would suggest to the skilled artisan that subcutaneous administration is desirable over IV administration. The invention could be reproduced with a reasonable expectation of success given that subcutaneous administration is taught by Jiang to be advantageous, Jiang explicitly suggests using said administration to treat human patients with HAE, and the art establishes that a 2 mL dose is a maximum volume for a subcutaneous dose

of a drug (i.e. requiring the Cinryze 1000 U dose to be at a concentration of 500 U/mL). The invention would be *prima facie* obvious to one of ordinary skill in the art at the time of invention.

With respect to claim 18, the dosage in Jiang is already taught in a range that would encompass the dosages as claimed if converted to normal subcutaneous dosage amounts. See above for the teaching that subcutaneous administration is limited to 2 mL. A dose of 800U to 1150U would by necessity be limited to 400 U/mL or 575 U/mL if formulated at the maximum 2 mL volume.

With respect to claim 20, the Jiang art teaches administration every three days as set forth above.

With respect to claim 21, the administration in Jiang is such that it encompasses up to three times a week as claimed (at 0, 3, and 6 days).

With respect to claim 32, the Jiang art establishes that blood levels of Cinryze are elevated after subcutaneous administration within 30 minutes, and remain stable/elevated for at least 3 days until the next dosage is administered. One of ordinary skill would expect similar results to occur with a higher dosing regimen required by the 2 mL subcutaneous volume limit.

With respect to claims 33-35, the Jiang art teaches that administration of Cinryze is for treatment and prophylaxis of HAE. HAE only has two isoforms (type I and type II) so by necessity Jiang must be treating those.

With respect to claim 46, the known use of Cinryze is for HAE attacks. The same route of administration and method of administration is found in the prior art. By

necessity, it must also result in a decrease in severity and/or number of attacks, as that is the known function of Cinryze. Furthermore, the combined prior art references result in the same dosage and administration route, so the resultant property of the method (decrease in severity and/or number of attacks) must necessarily result.

With respect to claim 47, Cinryze is known in the art to be purified from plasma.

With respect to claim 49, Cinryze is 100% identical to SEQ ID NO:1.

With respect to claim 50, by necessity the preparation of a subcutaneous dose would have to be in the form of a liquid formulation.

With respect to claim 51, it is known that Cinryze as used by Jiang is initially supplied as a lyophilized powder that must be reconstituted, as opposed to a pre-made liquid formulation.

With respect to claim 52, again since the same method and technique is used to deliver the same protein as claimed, the process would inherently result in the level of the C1 esterase inhibitor in the blood to increase to about 1 U/mL. See MPEP 2112.

***Response to Arguments:***

The Applicants argue that Jiang uses a low concentration of 100 U/mL, referencing the Schranz Declaration at ¶19. The Applicants also argue that the Frank declaration additionally establishes that the administration of Cinryze was at a dose of 100 U/mL. The Applicants argue the low dose would not provide a reasonable expectation of success, and that the clinical trials described by Anonymous and Kreuz demonstrate failure of such a dose. The Applicants argue that the Schranz declaration establishes difficulty in higher concentration of protein drugs. The Applicants argue that



there is high uncertainty as to whether Cinryze could be formulated at a high enough concentration for subcutaneous delivery, arguing that the consensus would be that it could not be formulated as such. The Applicants point out that the field was focused on low concentration formulations which were unsuccessful for subcutaneous administration. The Applicants argue that high volumes (for Anonymous) needed to be administered with a proprietary drug delivery platform based on human hyaluronidase enzyme, which was found not successful due to safety concerns. The Applicants argue that Kreuz showed similar large volumes. The Applicants argue that the invention cannot be obvious in view of the prior art, and discuss the current status of their subcutaneous administration efforts. The Applicants mention "unexpectedly good bioavailability". The Applicants state that a higher administration of Cinryze (1000 U at 100 U/mL) achieves 70% bioavailability as compared to a 50 U/mL injection having 40% bioavailability, and argue that this was unexpected because the increased viscosity of the formulation has no impact on absorption and tissue distribution. The Applicants argue that there is a long-felt need for the subcutaneous administration route. The Applicants' arguments have been considered but are not persuasive.

Firstly, the Examiner agrees with Applicants in that Jiang only teaches a dosage of 100 U/mL. However, as set forth above the general knowledge in the art concerning subcutaneous administration of drugs would motivate one of ordinary skill in the art to modify the dosage regimen of Jiang. Since a normal subcutaneous dose is at most 2 mL in volume, one of skill would seek to administer Cinryze at this level or lower, which would by necessity result in an increase in concentration from 100 U/mL to at least 400

U/mL as claimed. The Examiner agrees with the points from both the Schranz and Frank declarations concerning these dosage levels, but cannot ignore what is generally known in the art (volume limits of subcutaneous administration). There is a minor burden to modify the Jiang art in accordance with said known volume levels. There is no evidence that the higher concentration necessarily impacts syringeability or viscosity of the composition. While Cinryze is a large protein, larger 150 kDa proteins are known to be administered subcutaneously without major issues (see e.g. Table 1 in World J. Biol. Chem. 26:73-92, published April 2012). The Applicants have provided no actual evidence that the higher concentration posed technical problems beyond assertion/opinion in the remarks and declaration, which is insufficient to establish that the art found this to be a problem.

The Applicants are correct in that Anonymous and Kreuz would not provide for the claimed dose. However, the teachings of those pieces of prior art are irrelevant to the above rejection under Jiang and UNC, and the rejections under Anonymous and Kreuz have been withdrawn. As set forth *supra*, the UNC art provides motivation to seek a total volume of 2 mL or less. This would necessarily result in Jiang being modified to have the Cinryze be at a concentration of at least 400 U/mL. The teachings of Anonymous and Kreuz with respect to the instant rejection are irrelevant since they are not being recited as prior art reading upon the instant claims. Even considering that they might demonstrate later failure of a dose of 100 U/mL, such would motivate one of ordinary skill to seek other dosages, including higher dosages in an effort to ensure that

bioactive Cinryze reaches the bloodstream to act in a prophylactic or therapeutic manner for HAE patients.

The Examiner has considered the arguments found in Dr. Schranz's declaration concerning difficulty in higher concentration formulation. However, Dr. Schranz's declaration provides little more than an assertion that it is difficult to reach such a concentration formulation, as opposed to actual evidence establishing that this (1) was a recognized problem in the art and (2) was generally not achievable via other means. The art cited *supra* by the Examiner establishes that subcutaneous administration of proteins larger than Cinryze is known in the art (see e.g. the Table 1 in the World J. Biol. Chem. Art as cited, particularly Golimumab, Ustekinumab, Entercept, and Rilonacept). The apparent molecular weight of Cinryze is less than those proteins, which suggests that even considering the extra molecular weight provided by glycosylation, the problem of subcutaneous delivery of large proteins is not insurmountable.

Again, as to high concentration formulations, the Applicants have provided no direct evidence that it was considered a problem in the art. The Applicant's statements to that effect in the Declaration and Remarks are simply assertions not backed up by requisite evidence.

As to consideration that the art was focused on low concentration dosages that were found to be insufficient, as set forth *supra* this would motivate the skilled artisan to seek other dosages. Per *KSR*, "A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421, 82 USPQ2d 1385, 1397 (2007). "[I]n many cases a person of ordinary skill will be able

to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* at 420, 82 USPQ2d 1397. Office personnel may also take into account "the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418, 82 USPQ2d at 1396."

As to the argument that the prior art demonstrates use of a delivery system and high volumes, while this is true, this applies only to the Anonymous art. Jiang makes no mention of the hyaluronidase delivery system. Further, when combined with the required 2 mL injection volume of UNC, the volume is far lower than what is found in either Jiang or Anonymous. The same applies to Kreuz, which is not under consideration or part of the above rejection. While it might utilize higher volumes, the knowledge in the art of a 2 mL subcutaneous dosage motivates one of skill to modify Jiang.

The current status of the Applicants' invention (status in clinical trials) is not found to bear upon the instant rejection in the form of any secondary considerations that would preclude a rejection under 35 U.S.C. 103(a).

As to the allegations of unexpected results, firstly as set forth above the art demonstrates that subcutaneous formulations of large proteins (e.g. antibodies) are known. Further, those formulations demonstrate reasonable bioavailability (see e.g. Table 1 of the above World J. Biol. Chem. art). The allegation that the increase in concentration somehow unexpectedly still results in good bioavailability is not persuasive. One of skill would expect that if the dosage of a formulation is doubled, then a roughly double increase in bioavailability should result. Accordingly, the bioavailability

as admitted by the Applicants went from 40% at 50 U/mL to 70% at 100 U/mL. The Examiner does not find any reason why this result is unexpected.

Finally, as to the allegations of long felt need, the Examiner has considered the arguments combined with Dr. Schranz's declaration. Per MPEP 716.04, long felt need must satisfy a three-pronged test:

- 1. The claimed invention must satisfy a long-felt need which was recognized, persistent, and not solved by others.**
- 2. The invention must satisfy the long-felt need.**
- 3. The evidence must show unsuccessful efforts to solve the problem.**

The declaration and arguments merely provide assertions to satisfy prong #1. There is no evidence provided that the art generally considered this a long-felt need, which is required to demonstrate that the art as a whole considered the lack of a subcutaneous form of administration of a C1 esterase inhibitor to be a long-felt need. The Examiner agrees that the invention is highly useful and beneficial as a subcutaneous dose as compared to the standard intravenous administration route, but this does not in and of itself establish that the art recognized this as a persistent problem not solved by others. For instance, if the art established that previous attempts to high concentration of C1 esterase inhibitors failed due to solubility, syringability, etc. issues, then that might establish evidence of the long felt need not be satisfied by others. The second prong is found by the Examiner to be met by the instantly claimed invention. As to the final prong, there is no clear evidence that high concentration efforts have not been attempted unsuccessfully to solve the problem. As admitted by the

Applicants, all other art as cited by the Examiner was concerned with 100 U/mL or lower administration routes. There does not appear to be any evidence that establishes that high concentration subcutaneous administration was identified as a problem and unsuccessfully examined. Again, while the Declaration and arguments make a persuasive case as to why patients suffering from HAE would desire subcutaneous administration routes, neither provides sufficient evidence at this point to successfully establish long-felt need. The long-felt need may be present as alleged, but the arguments as such are right now merely assertions/opinions of a single expert, rather than evidence from the art as a whole that this is truly an art-recognized long felt need. As such, the allegations of long-felt need as a secondary consideration are not found to be sufficient to preclude a rejection under 35 U.S.C. 103(a).

The rejection is modified owing to the amendment and maintained.

**2. Claim 48** is rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over **Jiang** et al. (Clinical Immunology 136:323-328, published 8 June 2010) and **Anonymous** (The Pharmaceuticals and Compounding Laboratory: Subcutaneous at <http://pharmlabs.unc.edu/labs/parenterals/subcutaneous.htm>, published 14 June 2010) as applied to claim 16 above, and further in view of **Zuraw** (J. Allergy Clin. Immunol. 126:821-827.e.14, published October 2010, hereafter referred to as Zuraw).

The relevance of Jiang is set forth above. The difference between Jiang and the claimed invention is that Jiang does not teach that the C1 esterase inhibitor is recombinant.

Zuraw teaches that recombinant C1 inhibitor (rhC1INH) works for treatment of HAE (see e.g. Abstract). The administration of rhC1INH was at the known dosage and route as found for Cinryze (50 or 100 U/mL intravenously).

It would be obvious to one of ordinary skill in the art at the time of invention that recombinant C1 inhibitor as found in Zuraw could easily be substituted for Cinryze as found in Jiang, given that both are the same protein and only differ in their production routes. The skilled artisan would have a strong expectation that substitution of purified C1 inhibitor with recombinant C1 inhibitor would produce identical results since they are the same base protein. The invention would be *prima facie* obvious to one of ordinary skill in the art at the time of invention.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claim 53** is rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claim 53 is drawn to "The method of claim 54". There is no claim 54 present, thus it is not clear what are the metes and bounds of claim 53.

**II. Withdrawn Rejections:**

The rejection of claims 16-19, 21, 26-28, and 30-35 under 35 U.S.C. 102(a) as being anticipated by Anonymous is withdrawn in light of the amendment to the claims to recite the administration of "at least about 400 U/mL", which is not fairly taught by the Anonymous art, as well as the declaration of Dr. Schranz.

The rejection of claims 16-19, 21, 26-28, and 30-35 under 35 U.S.C. 102(a) as being anticipated by Kreuz is withdrawn in light of the amendment to the claims to recite the administration of "at least about 400 U/mL", which is not fairly taught by the Kreuz art, as well as the declaration of Dr. Schranz.

The rejection of claims 22, 23, 25, and 29 under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Anonymous and further in view of Jiang is withdrawn in light of the amendment to the claims, declarations of Drs. Schranz and Frank, and arguments.

***Conclusion***

No claims are allowed.

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

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not



mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY J. MIKNIS whose telephone number is (571)272-7008. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Alstrum-Acevedo can be reached on (571) 272-5548. 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.

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/Z. J. M./  
Examiner, Art Unit 1675

/CHRISTINA BRADLEY/  
Primary Examiner, Art Unit 1675