IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	: Roychowdhury *et al.*	Customer No.	: 62965
Serial No.	: 13/541,524	Confirmation No.	: 8238
Filed	: July 3, 2012	Group Art Unit	: 1629
Examiner	: Polansky, Gregg		
For	: DEXMEDETOMIDINE PREMIX FORMULATION		

RESPONSE TO OFFICE ACTION

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

Sir:

In response to the Office Action dated August 17, 2012, Applicants request consideration of the following remarks. Applicants believe no fee is due. However, if any fee is required in connection with this communication, please charge any deficiency, to Deposit Account No. 02-4377.

A Listing of the Claims begin on page 2 of this paper.

Remarks begin on page 3 of this paper.

LISTING OF THE CLAIMS

The listing of claims provided below will replace all prior versions and listings of claims in the application.

1. (Original) A ready to use liquid pharmaceutical composition for parenteral administration to a subject, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a concentration of about 0.005 to about 50 μg/mL disposed within a sealed glass container.

2. (Original) The ready to use liquid pharmaceutical composition of claim 1, wherein the dexmedetomidine or pharmaceutically acceptable salt thereof is at a concentration of about 0.05 to about 15 ug/mL.

3. (Original) The ready to use liquid pharmaceutical composition of claim 1, wherein the dexmedetomidine or pharmaceutically acceptable salt thereof is at a concentration of about 0.5 to about 10 ug/mL.

4. (Original) The ready to use liquid pharmaceutical composition of claim 1, wherein the dexmedetomidine or pharmaceutically acceptable salt thereof is at a concentration of about 1 to about 7 ug/mL.

5. (Original) The ready to use liquid pharmaceutical composition of claim 1, further comprising sodium chloride at a concentration of between about 0.01 and about 2.0 weight percent.

6. (Original) The ready to use liquid pharmaceutical composition of claim 5, wherein the sodium chloride is present at a concentration of about 0.9 weight percent.

7. (Original) The ready to use liquid pharmaceutical composition of claim 1, wherein the composition is formulated as a total volume selected from the group consisting of 20 mL, 50 mL and 100 mL.

REMARKS

Reconsideration is respectfully requested. Claims 1-7 are currently pending. No amendments have been introduced into the claims. Accordingly, no new matter has been introduced in this response.

I. Rejections Under 35 U.S.C. § 103(a)

A. U.S. Patent Application Publication No. 2011/0230534 as evidenced by a Precedex® Package Insert, U.S. Patent No. 6,806,291, U.S. Patent No. 5,716,988, and a Xylocaine® Package Insert

Claims 1-7 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent Application Publication No. 2011/0230534 to Miyawaki et al. (hereafter, "Miyawaki") as evidenced by the Precedex® Package Insert, U.S. Patent No. 6,806,291 to Sunkel et al. (hereafter, "Sunkel"), U.S. Patent No. 5,716,988 to Ibrahim et al. (hereafter, "Ibrahim"), and the Xylocaine® Package Insert.

The Examiner contends that Miyawaki discloses a kit for a ready to use parenterally administered local anesthesia, which allegedly includes a local anesthetic agent and dexmedetomidine or a salt thereof. According to the Examiner, the dexmedetomidine can be at a concentration of between $1x10^{-10}$ M and $1x10^{-6}$ M (*i.e.*, $2x10^{-5}$ µg/mL to 0.2 µg/mL), or at specific concentrations such as $4x10^{-6}$ M (*i.e.*, 0.8 µg/mL), wherein the dexmedetomidine is prepared from a Precedex® stock solution of dexmedetomidine hydrochloride that is diluted with 0.9% sodium chloride solution to achieve the desired dexmedetomidine concentrations. The Examiner alleges that the 0.8 µg/mL concentration of dexmedetomidine disclosed by Miyawaki reads on claim 4 because 0.8 µg/mL "is about 1 µg/mL," as recited by claim 4.

The Examiner concedes that Miyawaki does not suggest or describe disposing the parenteral compositions described by the reference within a sealed glass container. However, the Examiner relies on the Precedex® Package Insert, the Xylocaine® Package Insert, Sunkel and Ibrahim as evidence that disposing parenteral compositions in sealed glass containers is common and well known in the art. According to the Examiner, the Precedex® Package Insert describes a 100 µg/mL dexmedetomidine hydrochloride solution disposed within sealed glass vials that is diluted to 4 µg/mL with 0.9% sodium chloride solution for use. The Examiner also purports that the Xylocaine® Package Insert discloses a lidocaine HCl solution provided in glass ampoules and

vials at various concentrations and volumes. Further, the Examiner asserts that Sunkel discloses pharmaceutical compositions for parenteral administration, which may comprise dexmedetomidine, contained in glass ampoules and vials. Lastly, the Examiner alleges that Ibrahim discloses compositions comprising oxaliplatinum contained in 50 mL sealed glass vials.

The Examiner concludes that it would have been obvious to provide the diluted dexmedetomidine composition described by Miyawaki in sealed glass containers since it allegedly was a common and predictable method of providing parenteral pharmaceutical compositions. Furthermore, the Examiner contends that there are a limited number of options available with regard to the material for the container, and as such, the skilled artisan would envisage disposing the dilution in a glass container. Additionally, the Examiner alleges that it would have been obvious to use a sealed glass storage container to preserve the sterility of the dilution.

Applicants respectfully traverse the rejection. To support an assertion of obviousness, the Examiner must show 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." *See* M.P.E.P § 2143. *See also KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S. Ct. 1727, 82 (2007). Applicants submit that the claims are not obvious over the cited references because the combined disclosure of the cited references does not suggest or describe all of the claims elements. Furthermore, practicing the claims results in surprising and unexpected advantages with regard to stability of the claimed composition over the prior art, which is indisputable evidence of the non-obviousness of the claims over the cited references.

Independent claim 1 recites a ready to use liquid pharmaceutical composition for parenteral administration to a subject, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof at a concentration of about 0.005 to about 50 μg/mL disposed within a sealed glass container. In contrast to the claims, as conceded by the Examiner, Miyawaki does not suggest or describe that the diluted dexmedetomidine compositions recited by the reference are disposed within a sealed glass container. Rather, Miyawaki discloses a kit for the preparation of a composition for local anesthesia, wherein the composition includes a local anesthetic agent, and an α_2 receptor agonist, such as dexmedetomidine. The kit provides for the combination of components into a single composition in advance of its use for local anesthesia (*see* Miyawaki, page 2, paragraphs [0024] - [0031]; and page 9, paragraph [0095]).

Importantly, contrary to the Examiner's assertions, Applicants submit that none of the Precedex® Package Insert, Sunkel, Ibrahim or the Xylocaine® Package Insert provide an artisan of ordinary skill with guidance, suggestion, or motivation to prepare the diluted dexmedetomidine compositions described by Miyawaki in a sealed glass container.

With regard to the Precedex® Package Insert, the reference does not suggest or describe a composition comprising about 0.005 to about 50 μg/mL dexmedetomidine, or a pharmaceutically acceptable salt thereof, wherein the composition is disposed within a sealed glass container as a ready to use premixture. In contrast, the Precedex® Package Insert discloses a dexmedetomidine composition that is supplied as a 100 μg/mL concentration that must be diluted to 4 μg/mL prior to administration to a subject. (*See* the Precedex® Package Insert, page 1, col. 1). The reference does not suggest or describe that the dexmedetomidine would have been diluted into a sealed glass container. Rather, because the diluted composition is administered to a subject by an intravenous infusion (*see, e.g.,* the Precedex® Package Insert, page 1, col. 1), an artisan of ordinary skill would have diluted the dexmedetomidine in a device for infusion, such as a plastic infusion bag or plastic syringe, and would not have disposed the 4 μg/mL dilution into a sealed glass container. The Examiner provides no basis or evidence to suggest that an artisan of ordinary skill would have prepared the dilution in a sealed glass container as claimed. Furthermore, Applicants note that in rejecting the claims as allegedly being obvious over the Precedex® Package Insert (*see* the Office Action, item 8, page 9; and section I(C), below), the Examiner concedes that the Precedex® Package Insert does not suggest or describe disposing the diluted 4 μg/mL dexmedetomidine composition in a sealed glass container. Thus, in view of the Precedex® Package Insert, the artisan would not have been motivated to prepare the diluted dexmedetomidine composition described by Miyawaki in a sealed glass container.

Additionally, Applicants note that the Precedex® Package Insert describes dexmedetomidine compositions for intravenous administration to a subject. (*See* the Precedex® Package Insert, page 1, col. 1). In contrast, Miyawaki is directed to compositions for injection that produce a local anesthetic effect. (*See* Miyawaki, page 4, paragraph [0048]). Miyawaki does not suggest or describe that such compositions can be administered via an intravenous infusion. Thus, an artisan of ordinary skill would not have been motivated to combine the features of an intravenous formulation described by the Precedex® Package Insert with a composition formulated for local injection, as described by Miyawaki.

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