

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMNEAL PHARMACUTICALS LLC,
Petitioner,

v.

HOSPIRA INC.,
Patent Owner.

Case IPR2016-01580
Patent 8,648,106 B2

Before MICHAEL J. FITZPATRICK, SHERIDAN K. SNEDDEN, and
ZHENYU YANG, *Administrative Patent Judges*.

FITZPATRICK, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Petitioner, Amneal Pharmaceuticals LLC filed a Petition to institute an *inter partes* review of claims 1–9 of U.S. Patent No. 8,648,106 B2 (Ex. 1001, “the ’106 patent”) pursuant to 35 U.S.C. § 311(a). Paper 2 (“Pet.”). Patent Owner, Hospira Inc., filed a Preliminary Response under 35 U.S.C. § 313. Paper 9 (“Prelim. Resp.”).

We have authority to determine whether to institute an *inter partes* review. 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). Upon consideration of the Petition and Preliminary Response, and for the reasons explained below, we determine that the information presented does not show a reasonable likelihood that Petitioner would prevail with respect to any claim challenged in the Petition. *See* 35 U.S.C. § 314(a); 37 C.F.R. § 42.108. The Petition is denied.

A. Related Matters

Patent Owner has asserted the ’106 patent in *Hospira, Inc. v. Amneal Pharmaceuticals LLC*, No. 1:15-cv-00697 (D. Del.). Pet. 74; Paper 4, 2.

Petitioner has filed petitions for *inter partes* reviews of U.S. Patent Nos. 8,338,470 B1, 8,455,527 B1, and 8,242,158 B1, which are related to the ’106 patent. Pet. 6–7; *see also* Cases IPR2016-01578, IPR2016-01579, IPR2016-01577.

B. The ’106 Patent

4-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole is known shorthand as medetomidine. Ex. 1001, 1:26–27. It is a racemic mixture of two

enantiomers: levomedetomidine and dexmedetomidine. *Id.*; Ex. 2005 ¶25.¹ The '106 patent focuses on the latter enantiomer, dexmedetomidine, and “relates to patient-ready, premixed formulations of dexmedetomidine, or a pharmaceutically acceptable salt thereof, that can be used, for example, in perioperative care of a patient or for sedation.” Ex. 1001, 1:19–22.

The '106 patent acknowledges that, before the claimed invention, both medetomidine and dexmedetomidine were known to be α_2 -adrenoceptor agonists and used as antihypertensive, sedative, and analgesic agents. *Id.* at 1:28–50. The '106 patent also acknowledges prior patents disclosing medical administration of dexmedetomidine, including via epidural, parenteral, intravenous, oral, hypodermic, and transmucosal routes. *Id.* at 1:34–60 (citing various U.S. patents).

C. The Challenged Claims

Of the challenged claims, claim 1 is independent. It is illustrative and reproduced below.

1. A ready to use liquid pharmaceutical composition for parenteral administration to a subject, comprising dexmedetomidine or a pharmaceutically acceptable salt thereof disposed within a sealed glass container, wherein the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine.

D. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

¹ Exhibit 2005 is a declaration by Robert Linhardt, Ph.D.

References	Basis²	Claims
2010 Precedex Label (Ex. 1007) ³ and Palmgren (Ex. 1017) ⁴	§ 103(a)	1–9
Aantaa (Ex. 1006), ⁵ 2010 Precedex Label, and Palmgren	§ 103(a)	1–9
2010 Precedex Label, De Giorgi (Ex. 1015), ⁶ Eichhorn (Ex. 1016), ⁷ Palmgren, and Lavoisier (Ex. 1018) ⁸	§ 103(a)	1–9

Pet. 11–12.

² The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112-29, which was enacted September 16, 2011, made amendments to 35 U.S.C. §§ 102 and 103. AIA § 3(b) and (c). Those amendments became effective eighteen months later on March 16, 2013. *Id.* at § 3(n). Because the application from which the ’106 patent issued was filed before March 16, 2013, any citations herein to 35 U.S.C. §§ 102 and 103 are to their pre-AIA versions.

³ The 2010 Precedex Label is an FDA-approved label for Precedex, which is the commercial or brand name for dexmedetomidine-HCl. Ex. 1007, l. 7. Petitioner alleges it was published September 2010.

⁴ Palmgren, Joni J. et al., *Drug adsorption to plastic containers and retention of drugs in cultured cells under in vitro conditions*, 64 EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS 369–78 (June 29, 2006).

⁵ U.S. Patent No. 6,716,867 B1, issued April 6, 2004.

⁶ De Giorgi, Isabella et al., *Risk and pharmacoeconomic analyses of the injectable medication process in the paediatric and neonatal intensive care units*, vol. 22 no. 3 INTERNATIONAL JOURNAL FOR QUALITY IN HEALTH CARE 170–78 (2010).

⁷ Eichhorn, John H., *APSF Hosts Medication Safety Conference: Consensus Group Defines Challenges and Opportunities for Improved Practice*, vol. 25 no. 1 THE OFFICIAL JOURNAL OF THE ANESTHESIA PATIENT SAFETY 1, 3–8 (Spring 2010).

⁸ Lavoisier product sheet for NaCl 0.9% injectable solution (June 2009).

II. ANALYSIS

A. Claim Construction

“A claim in an unexpired patent that will not expire before a final written decision is issued shall be given its broadest reasonable construction in light of the specification of the patent in which it appears.” 37 C.F.R. § 42.100(b). Pursuant to that standard, the claim language should be read in light of the specification, as it would be interpreted by one of ordinary skill in the art. *In re Suitco Surface, Inc.*, 603 F.3d 1255, 1260 (Fed. Cir. 2010). Thus, we generally give claim terms their ordinary and customary meaning. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007) (“The ordinary and customary meaning ‘is the meaning that the term would have to a person of ordinary skill in the art in question.’” (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc))). A patentee, however, may rebut this presumption by acting as his own lexicographer, providing a definition of the term in the specification with “reasonable clarity, deliberateness, and precision.” *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

The parties propose express constructions for two limitations, “dexmedetomidine” and “ready to use,” both of which appear in claim 1 and are incorporated by the remainder of the claims of the ’106 patent. We need not construe these limitations, however, as a different limitation of claim 1 is dispositive of the Petition. That limitation is “wherein the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine.” As explained below, none of Petitioner’s grounds show

this limitation is met by the prior art.

B. Obviousness over 2010 Precedex Label and Palmgren

In assessing obviousness, “the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved.” *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966).⁹

1. Disclosure of 2010 Precedex Label

The 2010 Precedex Label is a drug label for Food and Drug Administration-approved “Precedex (dexmedetomidine hydrochloride) injection.” Ex. 1007, l. 7. It discloses Precedex “[f]or intravenous infusion following dilution.” *Id.* at line 8.

Precedex is supplied in 2mL glass vials at a concentration of 100 mcg/mL, which are “[s]tore[d] at controlled room temperature, 25°C (77°F) with excursions allowed from 15 to 30°C (59 to 86°F).” *Id.* at ll. 698–701. The drug “must be diluted in 0.9% sodium chloride solution to achieve required concentration (4 mcg/mL) prior to administration.” *Id.* at ll. 175–76.

⁹ Additionally, secondary considerations such as “commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.” *Graham*, 383 U.S. at 17–18. In its Preliminary Response, however, Patent Owner does not argue that any secondary considerations evidence supports non-obviousness of the challenged claims.

2. *Disclosure of Palmgren*

Palmgren discloses results of experiments on adsorption of certain acidic and basic drugs to various containers. Ex. 1017, Abstract. Palmgren reported that loss in basic drugs, including medetomidine, to polystyrene and polycarbonate was much higher than to glass and polypropylene tubes. *Id.* at 374.

3. *Application of the Prior Art to the Challenged Claims*

Petitioner argues that the subject matter of claims 1–9 would have been obvious to a person of ordinary skill in the art in view of the teachings of the 2010 Precedex Label and Palmgren. Pet. 15–31. In brief, Petitioner argues that a person of ordinary skill in the art would have diluted Precedex, according to the 2010 Precedex Label, to a liquid composition having a dexmedetomidine-HCl concentration of 4 mcg/mL, which would make the drug “ready to use” (*see, e.g.*, Ex. 1001, 2:19–21, 26:41–43 (claim 6)) and contain the so-diluted liquid in a “sealed glass container,” thereby satisfying those limitations of claim 1. *Id.* at 17–19.

Claim 1, however, additionally recites “wherein the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine.” Petitioner presents various arguments with respect to this limitation but none is sufficient. *Id.* at 20–23.

First, Petitioner argues that “Precedex™ concentrate disclosed in the 2010 Precedex Label was determined to be stable for two years.” *Id.* at 20 (citing Ex. 1013, 8). This argument is inapposite because it speaks to the

concentrated form of dexmedetomidine-HCl disclosed in the 2010 Precedex Label, which is outside the scope of claim 1, and not to a “ready to use” diluted form. Moreover, Petitioner has not shown that “stable” is equivalent in meaning to “no more than about 2% decrease in the concentration of dexmedetomidine,” as recited in claim 1. In fact, Petitioner’s own understanding of “stable” affords up to a 10% decrease in concentration. *See id.* at 20–21 (“Based on FDA requirements for drug stability, one of skill in the art would expect at most a 10% decrease in concentration.”) (citing Ex. 1003 ¶¶66–68).

Second, Petitioner reargues that a person of ordinary skill in the art would have a reason to use a glass container for the “ready to use” dexmedetomidine-HCl composition because glass yields superior stability results. Pet. 21. We agree with that proposition, but it does not account for the limitation at issue—that “the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine.”

Third, Petitioner asserts that this limitation is inherently met, stating: “It is irrelevant that the 2010 Precedex Label does not explicitly disclose this inherent property of the Precedex® solutions therein.” Pet. 22. But, like its “stable for two years” argument, Petitioner’s inherency argument speaks to the concentrated form of dexmedetomidine-HCl disclosed in the 2010 Precedex Label, which is outside the scope of claim 1, and not to a “ready to use” diluted form. Moreover, the stated basis for Petitioner’s inherency assertion is that “the Precedex™ solutions disclosed in the 2010 Precedex Label were stored under identical conditions – sterile, in a sealed glass

container – as those in Example 1 of the '106 patent which exhibited no more than about 2% decrease in the concentration.” *Id.* at 22 (citing Ex. 1001, 13:35–43; Ex. 1007, ll. 207–08, 697–701). But, the conditions were not identical; they employed different concentrations and temperatures. More specifically, the 2010 Precedex Label discloses glass vial storage of dexmedetomidine-HCl at a concentration of 100 mcg/mL concentration and a temperature of “25°C (77°F) with excursions allowed from 15 to 30°C (59 to 86°F),” whereas Example 1 of the '106 patent presents five-month stability data for dexmedetomidine-HCl at a concentration of just 4 mcg/mL and at a temperature of 40°C. *Compare* Ex. 1007, lines 697–701, *with* Ex. 1001, 13:28–37, 45–47, 14:4–14.

Further, Example 1 of the '106 patent indicates that the difference in temperature, from 40°C to 25°C, is quite significant to the stability of dexmedetomidine-HCl. As part of Example 1, concentration loss of dexmedetomidine-HCl was measured after two weeks of glass vial storage at 25°C, which is the only time duration that was tested at 25°C. Ex. 1001, 14:4–14. The measured loss was 1.8%. *Id.* at 14:14 (reporting 98.2% potency). In contrast, only 0.6% was lost after 1 month of glass vial storage at 40°C, which is the shortest time duration tested at 40°C. *Id.* at 14:14 (reporting 99.4% potency).

In sum, Petitioner has not shown that the relied-upon prior art teaches “wherein the liquid pharmaceutical composition when stored in the glass container for at least five months exhibits no more than about 2% decrease in the concentration of dexmedetomidine,” or that it is inherent. That limitation is recited by claim 1 and incorporated by all other challenged

claims via their dependency on claim 1. Accordingly, there is not a reasonable likelihood of Petitioner prevailing in challenging any of claims 1–9 as unpatentable over 2010 Precedex Label and Palmgren.

C. The Remaining Grounds

Petitioner challenges claims 1–9 as unpatentable over Aantaa, the 2010 Precedex Label, and Palmgren as well as over the 2010 Precedex Label, De Giorgi, Eichhorn, Palmgren, and Lavoisier. Pet. 11–12. In both of these additional grounds, Petitioner relies on the same flawed inherency argument. *See* Pet. 37–38, 56. Accordingly, there likewise is not a reasonable likelihood of Petitioner prevailing in challenging claims 1–9 on either of these remaining grounds.

III. CONCLUSION

We have considered the information presented in the Petition and Preliminary Response and determine that there is not a reasonable likelihood that Petitioner would prevail with respect to any claim challenged in the Petition. *See* 35 U.S.C. § 314(a); 37 C.F.R. § 42.108.

IV. ORDER

Accordingly, it is
ORDERED that the Petition is denied.

IPR2016-01580
Patent 8,648,106 B2

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