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Paper No. 9
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

COALITION FOR AFFORDABLE DRUGS XI LLC,
Petitioner,

v.

INSYS PHARMA, INC.,
Patent Owner.

Case IPR2015-01800
Patent 8,486,972 B2

Before DEBORAH KATZ, GRACE KARAFFA OBERMANN, and SUSAN L. C. MITCHELL, *Administrative Patent Judges.*

OBERMANN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner requests an *inter partes* review of claims 1–3 of U.S. Patent 8,486,972 B2 ("the '972 patent"). Paper 1 ("Pet."). Patent Owner filed a Preliminary Response. Paper 8 ("Prelim. Resp."). We have statutory authority under 35 U.S.C. § 314(a), which provides that an *inter partes* review may not be instituted unless the Petition demonstrates "a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Taking account of the information presented in the Preliminary Response, we conclude that the Petition fails to make that showing. On this record, we deny the Petition and decline to institute review.

A. Related Proceedings

Petitioner identifies no related district court proceedings. Pet. 3. With this decision, we issue decisions denying *inter partes* review in IPR2016-01797 and IPR2016-01799, which involve the same parties and related patents.

B. The '972 Patent

The '972 patent relates to a sublingual formulation of fentanyl, an opioid receptor agonist with analgesic potency up to 100 times that of morphine. Ex. 1001, 1:12–13. Sublingual delivery is achieved through the mucosal membranes lining the floor of the mouth. *Id.* at 8:23–24. The '972 patent describes a sublingual formulation of fentanyl useful for relieving "breakthrough pain" in cancer patients almost immediately after administration. *Id.* at 6:26–39.

The '972 patent distinguishes sublingual (floor of the mouth) administration from other routes of delivery, for example, buccal (lining of the cheeks) administration. *Id.* at 7:58–8:29. The specification recognizes solid (such as lozenge) and liquid (such as spray pump) forms of sublingual fentanyl. *Id.* at 1:59–61; 9:9–12. The '972 patent discloses a fentanyl formulation delivered "to

the sublingual mucosa via spray," which "results in a rapid onset of therapeutic effect of" the active agent. *Id*. at 9:43–45.

C. Illustrative Claim

Claims 1, the only independent claim, is illustrative and reads as follows:

> 1. A unit dose of a non-propellant sublingual fentanyl formulation comprising discrete liquid droplets of an effective amount of fentanyl and a pharmaceutically acceptable liquid carrier, wherein the sublingual fentanyl formulation comprises:
>
> from about 01.% to about 0.8% by weight of fentanyl or a pharmaceutically acceptable salt thereof; from about 20% to about 60% weight of ethanol; and from about 4% to about 6% by weight of propylene glycol;
>
> wherein after sublingual administration to a human, said sublingual fentanyl formulation provides a mean time to maximum plasma concentration (T*max*) of fentanyl of from about 5 to about 120 minutes.

D. The Asserted Prior Art

The Petition asserts the following references in the grounds of unpatentability:

1. UK Patent App. No. GB 2399286 A, pub. Sept. 15, 2004. (Ex. 1003) ("Ross GB").

2. US Patent Pub. No. 2006/0062812 A1, pub. Mar. 23, 2006 (Ex. 1005) ("Ross US").

3. US Patent No. 5,370,862, issued Dec. 6, 1994 (Ex. 1004) ("Klokkers-Bethke").

4. US Patent Pub. No. 2002/0055496 A1, pub. May 9, 2002 (Ex. 1006) ("McCoy").

E. Asserted Grounds of Unpatentability

The Petition asserts the following grounds of unpatentability:

References	Basis	Claim(s) Challenged
Ross GB, Ross US, and Klokkers-Bethke	§ 103	1, 3
Ross GB, Ross US, Klokkers-Bethke, and McCoy	§ 103	2

In addition to the asserted prior art references, the Petition advances declaration testimony of Dr. Kinam Park. Ex. 1002.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, we construe claim terms of an unexpired patent according to their broadest reasonable interpretation in light of the patent specification. 37 C.F.R. § 42.100(b). Under that standard, we assign terms their ordinary and customary meaning as understood by one of ordinary skill in the art in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994). We construe only those terms necessary to resolve the controversy. *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

No claim term requires express construction for the purposes of this decision. The prior art, itself, demonstrates the appropriate level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (the prior art, itself, can reflect the level of skill in the art).

B. A Problem Common to Both Grounds Asserted in the Petition

A problem common to both grounds asserted in the Petition is a failure to identify a persuasive reason why a person of ordinary skill in the art would have been prompted to combine the various elements of the prior art in the precise fashion required by the challenged claims. "[A] patent 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). "If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Obviousness can be established when the prior art, itself, would have suggested the claimed subject matter. *In re Rinehart*, 531 F.2d 1048, 1051 (CCPA 1976). But the Petition identifies no persuasive reason why the prior art would have recommended the combination of elements upon which the challenges depend. In that regard, the Petition strives to identify each element of the claims, from among disparate disclosures in the art, but neglects to explain adequately why one would have selected and combined those particular features to arrive at the sublingual fentanyl formulation required by the challenged claims. The Petition is replete with examples of that deficiency. We focus our analysis on one example, which is dispositive and requires denial of review.

C. The Propylene Glycol Limitation of Claims 1, 2, and 3

Claim 1 is directed to a sublingual fentanyl formulation comprising fentanyl (or a pharmaceutically acceptable salt thereof), ethanol, and propylene glycol in specified weight-percent amounts. Claims 2 and 3 depend from claim 1 and, thus, inherit those limitations. The Petition relies on the combined disclosures of

Ross GB and Klokkers-Bethke to establish the obviousness of the limitation that requires "from about 4% to about 6% by weight" of propylene glycol.

The Petition relies on a modification to Example 1 in Ross GB, which discloses a formulation that includes fentanyl base, saccharin, ethanol, menthol, and citrate buffer—but no propylene glycol. Pet. 30–34 (citing Ex. 1003, 11:1–9 (Ross GB's Example 1)). For the teaching of the propylene glycol limitation, Petitioner directs us to two disclosures in Ross GB that relate to propylene glycol; first, as a suitable solubility enhancer for fentanyl (Ex. 1003, 5:1–4), and second, as a suitable moisturizing agent (*id.* at 7:11–14). Pet. 31–32. The Petition does not identify in Ross GB any disclosure or suggestion of a weight-percent range of propylene glycol that would be useful in Ross GB's Example 1 formulation. *Id.*

Instead, the Petition directs us to Klokkers-Bethke's disclosure of propylene glycol in a nitroglycerin formulation for treating angina. Pet. 32; Ex. 1004, Title, 1:16–18. The Petition identifies no disclosure in Klokkers-Bethke that mentions fentanyl or pain management. Pet. 30–34. The Petition ignores that Ross GB's fentanyl formulation is "preferably free of any propellant," whereas Klokkers-Bethke's nitroglycerin formulation is delivered via a closed and charged aerosol canister and, thus, includes propellant. Ex. 1003, 4:1; *see* Ex. 1004, Abstract, 3:20–23, 4:2, 6:10; Prelim Resp. 14 (discussing that distinction between the applied references) (citations omitted).

The Petition identifies Klokkers-Bethke's disclosure of a "broad range of 2% to 30% by weight" for propylene glycol in the aerosol nitroglycerin formulation, and then argues, without adequate analysis, that an ordinary artisan, by routine experimentation, would have modified that range in the nitroglycerin formulation to reach an optimal range "of about 4% to about 6%" by weight. Pet. 32–34. The Petition does not direct us to a disclosed purpose for propylene

glycol in Klokkers-Bethke's nitroglycerin formulation—for example, a purpose comparable to one described for the fentanyl formulation of Example 1 in Ross GB. *Id.* at 31–33. The closest the Petition comes to identifying some reason that would have prompted one to import the optimized weight-percent of propylene glycol from the propellant-containing nitroglycerin formulation of Klokkers-Bethke, into the propellant-free fentanyl formulation of Ross GB, is in the argument that both formulations are "used in emergencies when the medication should be fast acting." *Id.* at 33 (quoting Ex. 1002 ¶ 24).

Critically lacking is any objective evidence—for example, a suggestion in the prior art—that a person of ordinary skill in the art would have understood that the amount of propylene glycol, optimized for use in an aerosol nitroglycerin formulation, would match the optimal amount of propylene glycol, useful in a propellant-free fentanyl formulation. *Id.* at 32–34. The Petition fails to address adequately how the compositional differences between the disparate formulations of Ross GB and Klokkers-Bethke would have informed that understanding. *Compare* Ex. 1003, 11:1–9 (Example 1 of Ross GB includes fentanyl, saccharin, ethanol, menthol, and citrate buffer), *with* Ex. 1004, 3:65–4:8 (Klokkers-Bethke's formulation includes nitroglycerin, ethanol, propylene glycol, and propellant).

Even if we set aside those shortcomings, the Petition is still deficient. As Patent Owner points out, the Petition is silent on "how the percentage by weight of propylene glycol in a closed and charged aerosol canister would change upon dispensation, prior to sublingual delivery." Prelim. Resp. 14. The Petition also fails to take into account how the addition of propylene glycol would upset the weight-percent amounts of fentanyl or ethanol in Ross GB's Example 1 formulation, upon which the Petition relies for disclosure of the other weight-percent limitations of the challenged claims. Pet. 30–34.

Ross GB discloses that propylene glycol is useful in fentanyl formulations that are "free of [] alcohol." Prelim. Resp. 17 (quoting Ex. 1003, 5:14–15). Ross GB's Example 1 formulation comprises "40% by weight of ethanol." Pet. 31; Ex. 1003, 11:1–9 (Example 1). Petitioner does not explain adequately why one would have imported Klokkers-Bethke's optimized amount of propylene glycol into the ethanol-containing formulation of Ross GB's Example 1.

In sum, the information presented does not show sufficiently that an ordinary artisan would have modified the formulation of Ross GB's Example 1 to include propylene glycol in a weight-percent amount that satisfies claims 1, 2, or 3. Both grounds asserted in the Petition depend upon that modification. Pet. 31–33. On this record, the Petition fails to establish a reasonable likelihood of prevailing with respect to claim 1, 2, or 3.

III. CONCLUSION

Taking account of the information in the Petition and Preliminary Response, we decline to institute review because the information presented does not demonstrate a reasonable likelihood that Petitioner would prevail with respect to at least one of the claims challenged in the Petition. 35 U.S.C. § 314(a).

IV. ORDER

For the reasons given, it is

ORDERED that the Petition is *denied*.

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