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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 IPR2015-01799
Patent 8,835,460 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 1–5 of U.S. Patent 8,835,460 B2 ("the '460 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. 2–3. With this decision, we issue decisions denying *inter partes* review in IPR2016-01797 and IPR2016-01800, which involve the same parties and related patents.

B. The '460 Patent

The '460 patent relates to a sublingual formulation of fentanyl, an opioid receptor agonist with analgesic potency up to 100 times that of morphine. Ex. 1001, 1:13–14. Sublingual delivery is achieved through the mucosal membranes lining the floor of the mouth. *Id*. at 8:27–28. The '460 patent describes a sublingual formulation of fentanyl useful for relieving "breakthrough pain" in cancer patients almost immediately after administration. *Id*. at 6:29–42.

The '460 patent distinguishes sublingual (floor of the mouth) administration from other routes of delivery, for example, buccal (lining of the cheeks) administration. *Id*. at 7:49–8:33. The '460 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 9:46–49. The formulations are

"delivered as liquid droplets having a mean diameter of at least about 10 microns," with a preferred distribution "from about 30 microns to about 70 microns." *Id*. at 9:36–45.

C. The Challenged Claims

Petitioner challenges claims 1–5 of the '460 patent. Critical to our analysis, each challenged claim relates to a sublingual fentanyl formulation in the form of liquid "droplets having a mean diameter" that falls within specified ranges. Claim 1 is illustrative and reads as follows (emphasis added):

> 1. A sublingual formulation comprising discrete liquid droplets of an effective amount of fentanyl or a fentanyl derivative selected from the group consisting of sufentanil, carfentanil, lofentanil and alfatenil,[1] a free base or a pharmaceutically acceptable salt thereof, in a pharmaceutically acceptable liquid carrier, *said droplets having a mean diameter of from about 30 to about 70 microns*.

Claims 2 and 3 require a non-propellant sublingual fentanyl formulation comprising discrete liquid "droplets having a mean diameter of at least about 10 microns." Claim 4 requires liquid "droplets having a mean diameter of from about 30 to about 70 microns." Claim 5 depends from claim 1 and, thus, inherits the limitation that requires discrete liquid "droplets having a mean diameter of from about 30 to about 70 microns."

D. The Asserted Prior Art

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

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

[1] The '460 patent specification discloses that the fentanyl derivative intended is alfentanil. Ex. 1001, 6:26–28; 18:29, 40.

2. US Patent Pub. No. 2002/0055496 A1, pub. May 9, 2002 (Ex. 1005) ("McCoy").

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

4. US Patent No. 6,946,150 B2, issued Sept. 20, 2005 (Ex. 1007) ("Whittle").

D. Asserted Grounds of Unpatentability

The Petition asserts the following grounds of unpatentability:

References	**Basis**	**Claim(s) Challenged**
Ross GB and McCoy	§ 103	1, 4, 5
Ross GB, Klokkers-Bethke, and McCoy	§ 103	2, 3
Ross GB and Whittle	§ 103	1, 4, 5
Ross GB, Klokkers-Bethke, and Whittle	§ 103	2, 3
McCoy	§ 102(b)	1, 4, 5

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).

The broadest reasonable interpretation of "discrete liquid droplets" requires express construction. That term is not defined, but is closely associated with the term "spray," in the '460 patent specification. Ex. 1001, 3:17–20 (invention is directed to "a liquid spray formulation in the form of discrete liquid droplets"). Based on the information presented, we accept Petitioner's view that the broadest reasonable interpretation of "discrete liquid droplets" is "water or other liquid broken up into minute droplets and blown, ejected into, or falling through the air." Pet. 14 (quoting Ex. 1008) (dictionary definition of "spray"). That interpretation is reasonable in view of the claim wording, the specification, and the dictionary definition of "spray" advanced by Petitioner. No other claim term requires express construction for the purposes of this decision.

B. Grounds Based on Obviousness

The Petition states four grounds of obviousness based on various combinations of asserted prior art references. Pet. 5–6. We focus on a single dispositive issue; namely, whether the information presented shows sufficiently that the asserted prior art references would have recommended, to one of ordinary skill in the art, modifying Ross GB's "spray" formulation to provide "droplets having a mean diameter" within the specified ranges of the challenged claims.

We first address whether Ross GB's reference to a "spray" formulation constitutes disclosure of "discrete liquid droplets." *Id*. at 19. We then turn to whether Petitioner shows sufficiently that an ordinary artisan would have been led

to modify Ross GB's "spray" to provide "droplets having a mean diameter" that falls within the specified ranges of the claims. *Id*. at 20–21 (argument as to claim 1). 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).

i. Ross GB's Reference to a "Spray" Formulation Constitutes Disclosure of "Discrete Liquid Droplets"

Each challenged claim requires a fentanyl formulation comprised of liquid droplets. Ex. 1001, 57:37–58:55 (claims 1–5). Claims 1–3 and 5 specify "discrete liquid droplets," whereas claim 4 specifies "liquid droplets." *Id*. The Petition directs us to Ross GB's disclosure of a "spray" formulation, which according to Petitioner, satisfies those liquid droplet limitations. Pet. 19–20 (quoting Ex. 1003, 3:29–33). Patent Owner responds that Ross GB's "spray" formulation is not shown adequately to comprise "discrete liquid droplets" or "liquid droplets" within the meaning of the claims. Prelim. Resp. 15–17.

Taking account of the information presented in the Petition and Preliminary Response, we determine that Ross GB's disclosure of a "spray" refers to a formulation that comprises "discrete liquid droplets." Pet. 19–20. Patent Owner aptly observes that Ross GB "does not use the words 'droplet,' 'discrete,' or any variant thereof." Prelim. Resp. 16. Notwithstanding that observation, the reference repeatedly refers to the administration of a fentanyl formulation "by means of a pump spray device." Ex. 1003, Abstract; *see id*. at 1:3–4 (Ross GB, disclosing "pump spray formulations" of fentanyl suitable for sublingual delivery); *id*. at 8:15 (packaging "multiple doses" of fentanyl preparations "in a pump spray system comprising a sealed container fitted with a metering pump").

The Petition directs us to Dr. Park's opinion that a person of ordinary skill in the art "would have understood that the spray disclosed in [Ross GB] comprises discrete liquid droplets." Pet. 19 (quoting Ex. 1002 ¶ 16). The Petition also identifies objective support for that opinion; specifically, a dictionary definition, which indicates that a "spray" would have been understood at the time of the invention to mean "water or other liquid broken up into minute droplets and blown, ejected into, or falling through the air." *Id*. at 14, 20 (quoting Ex. 1008).

Patent Owner suggests that Ross GB's "spray" reasonably refers to "a singular 'jet' of liquid" as demonstrated by two other definitions of "spray" set forth in the dictionary advanced by Petitioner. Prelim Resp. 15–16 (citing Ex. 1008). One definition refers to "a jet of fine particles of liquid." Ex. 1008. The next-stated definition refers to "a liquid to be discharged or applied in *such a jet*"—which reasonably refers back to the "jet of fine particles of liquid" referenced in the immediately prior definition. *Id*. (emphasis added). Both definitions advanced by Patent Owner, in fact, support Petitioner's view that a spray comprises "fine particles of liquid." *Id*. Neither refers to a "singular" jet of liquid. Prelim. Resp. 16; *see* Ex. 1008 (dictionary definitions). On this record, we determine that Ross GB's reference to a fentanyl "spray" would have conveyed to an ordinary artisan a liquid formulation broken up into minute droplets, within the meaning of the term "discrete liquid droplets" in claim 1.

We next turn to whether Petitioner shows sufficiently that one would have been prompted to modify the mean diameter of the droplets in Ross GB's spray formulation to provide a mean diameter within the ranges specified in the challenged claims.

ii. The Prior Art Is Not Shown to Recommend Modifying Ross GB's Spray to Provide "Droplets Having a Mean Diameter" Within the Claimed Ranges

Each challenged claim requires liquid "droplets having a mean diameter" that falls within specified ranges. Ex. 1001, 57:37–58:55 (claims 1–5). Claims 1, 4, and 5 specify "droplets having a mean diameter of from about 30 to about 70 microns." *Id*. Claims 2 and 3, by contrast, specify "droplets having a mean diameter of at least about 10 microns." *Id*. In Petitioner's view, the asserted prior art references would have recommended modifying Ross GB's spray formulation, in view of McCoy or Whittle, to provide "droplets having a mean diameter" within the claimed ranges. Pet. 19–51.

McCoy discloses a formulation and system for intra-oral delivery of pharmaceutical agents, including fentanyl, that are mixed with an oral-absorption enhancer. Ex. 1005, Abstract, ¶¶ 5, 17. McCoy discloses liquid droplets "sized within the range of about 1 to 200 microns, more preferably within the range of 10–100 microns." *Id*. ¶ 19. Whittle, by contrast, relates to a formulation of cannabinoids administered "via a pump action spray." Ex. 1007, Abstract. The Petition directs us to Whittle's disclosure of a cannabinoids-containing formulation delivered as a "spray in which the particles have a mean aerodynamic particle size of between 15 and 45 microns, more particularly between 20 and 40 microns and an average of about 33 microns." Pet. 41–42 (quoting Ex. 1007, 4:46–52).

The Petition includes no adequate rationale why a person of ordinary skill in the art would have been prompted to modify Ross GB's spray formulation to provide droplets sized according to McCoy or Whittle. Ross GB is not shown to be concerned with the size, much less the mean diameter, of liquid droplets in the spray formulation. *Id*. at 21–22. Even if we accept that McCoy or Whittle would have suggested liquid droplets having the specified mean diameter, institution of

review is not warranted, because the Petition does not explain adequately why one would have been led to import the droplet sizing disclosed in McCoy or Whittle into the spray formulation of Ross GB.

"[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 modifying Ross GB's spray to alter the size, or mean diameter, of the droplets. Instead, the Petition selects elements from compositionally-different formulations and, without addressing those differences, argues that it would have been obvious to combine the selected elements in the manner that is specified in the challenged claims.

Petitioner first argues that reducing the droplet size in Ross GB's spray, to a size comparable to the droplets disclosed in McCoy or Whittle, would have been understood to provide "a higher surface area to be absorbed by the mucosa of the intra-oral cavity." Pet. 22 (discussing McCoy) (quoting Ex. 1002 ¶ 22); *see id.* at 42 (discussing Whittle) (quoting Ex. 1002 ¶ 67). The Petition, however, fails to direct us to any disclosure in the asserted prior art, or any other credible evidence, from which we can reasonably conclude that an "ordinary artisan would have perceived the droplet sizes disclosed in" McCoy or Whittle to be smaller than those in Ross GB's spray. Prelim. Resp. 20. That deficiency, standing alone, warrants denial of the obviousness grounds stated in the Petition.

The Petition also fails to direct us to persuasive information that the mean diameter of droplets was of any concern in Ross GB's spray—much less that one would have understood that Ross GB's sublingual fentanyl spray would benefit from a modification to droplet surface area for the purpose of providing "a higher surface area to be absorbed by the mucosa of the intra-oral cavity." Pet. 22, 42. In that regard, McCoy's disclosure of droplet sizes is presented in the context of an intra-oral formulation that comprises an oral-absorption enhancer. Ex. 1005 ¶ 19. Whittle's disclosure of droplet sizes is presented in the context of a formulation containing cannabinoids, and is not shown on this record to address increasing the surface area for absorption by mucosa. Pet. 42; *see* Ex. 1007, Abstract, 4:40–53 (disclosure of preferred range of particle sizes for "delivering cannabinoids").

The Petition directs us to no credible information that links a concern—about droplet size, mean diameter, or droplet surface area—to Ross GB's spray, which includes no absorption enhancer and no cannabinoid. *See* Pet. 21–22, 42–43 (failing to establish that link, and directing us to no disclosure in Ross GB of a formulation comprising an absorption enhancer or a cannabinoid). That aspect of the Petition rests on bare opinion testimony that is not tethered adequately to objective evidence, tending to show that one would have combined the teachings of the references. *Id*. (citing Ex. 1002 ¶¶ 22–24, 67–68).

The Petition also includes argument that utilizing a smaller droplet size in Ross GB's spray would have been understood to decrease "any discomfort to the patient from administration of the drug." *Id*. at 22, 26 (quoting Ex. 1002 ¶ 23). Here again, the Petition directs us to no suggestion in the asserted prior art that one would have perceived the droplet sizes in Ross GB's spray to be larger than the droplets disclosed in McCoy or Whittle. *See* Prelim. Resp. 20. Nor does the Petition direct us to any disclosure sufficient to show that patient discomfort was a

concern in Ross GB. Pet. 22, 26, 35–36, 43, 49; *see* Prelim. Resp. 20–21 (pointing out that deficiency in the Petition).

On that point, Petitioner again rests on bare opinion testimony to make out its challenge. Pet. 22, 26, 35–36, 43, 49. Under our rules, however, an opinion that does not disclose underlying facts "is entitled to little or no weight." 37 C.F.R. § 42.65(a); *see Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 294 (Fed. Cir. 1985) (lack of objective support for opinion testimony "may render the testimony of little probative value in a validity determination"); *see also* Prelim. Resp. 19–22 (explaining why neither of the two asserted reasons for the proposed combination are adequately supported). Because the Petition rests on opinion testimony untethered to adequate objective proof—for example, disclosures in the prior art—institution of review is not warranted.

The obviousness grounds based on McCoy are deficient for another reason, which we discuss below in the context of the ground based on anticipation. In a nutshell, the Petition ignores that McCoy nowhere refers to the "mean diameter" of liquid particles. Pet. 25, 35, 54, 58; *see* Prelim. Resp. 17–19 (identifying that deficiency in the Petition). The Petition does not explain adequately how or why McCoy would have suggested the "mean diameter" limitations of the challenged claims. Ex. 1001, 57:37–58:55 (claims 1–5).

On this record, the Petition fails to show sufficiently that McCoy or Whittle would have recommended modifying the droplets in Ross GB's spray to satisfy the "mean diameter" limitations of claims 1–5. For that reason, the Petition fails to establish a reasonable likelihood of prevailing on the obviousness grounds.

C. The Ground Based on Anticipation by McCoy

The Petition asserts also that McCoy anticipates claims 1, 4, and 5. Pet. 51–60. Each of those claims requires liquid "droplets having a mean diameter of from

about 30 to about 70 microns." Ex. 1001, 57:37–58:55. The Petition fails to direct us to disclosure in McCoy that anticipates that specified range. Pet. 51–60.

The Petition directs us to McCoy's teaching that the liquid droplets will be "sized within the range of about 1 to 200 microns, more preferably within the range of 10–100 microns." *Id*. at 54 (quoting Ex. 1005 ¶ 19). Significantly, the Petition ignores that McCoy does not teach a "mean diameter" value or range for liquid droplets. *Id*. As Patent Owner points out, the Petition does not "explain how one of ordinary skill [in the art] would identify a particular range for mean diameter of droplets from a spectrum of possible droplet sizes that is about 2–5 times broader" than the mean diameter range "of from about 30 to about 70 microns" that is specified in claims 1, 4, and 5. Prelim. Resp. 51. In that regard, the Petition directs us to conclusory opinion testimony that McCoy's preferred droplet sizes encompass the claimed "mean diameter" range of claim 1. Pet. 54 (citing Ex. 1002 ¶ 21).

Patent Owner responds, and we agree, that the Petition fails to adequately explain how McCoy's preferred droplet sizes correspond to a mean diameter value, which "would require information regarding *distribution* of droplet diameters across the broad spectrum of droplet sizes" disclosed in McCoy. Prelim. Resp. 51. Critically lacking is a cogent explanation of how an ordinary artisan "would have predicted a particular range for mean diameter of droplets from a spectrum of possible droplet sizes" disclosed in McCoy. *Id*. at 17. We agree with Patent Owner that Dr. Park's sweeping, but unsupported, opinion that "there is no reasonable difference in how the claimed range operates over the range" disclosed in McCoy is insufficient to support a successful anticipation challenge. *Id*. at 18–19 (quoting Ex. 1002 ¶ 21).

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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