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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELI LILLY AND COMPANY.,
Petitioner,

v.

LOS ANGELES BIOMEDICAL RESEARCH INSTITUTE
AT HARBOR-UCLA MEDICAL CENTER,
Patent Owner.

Case IPR2014-00693
Patent 8,133,903 B2

Before LORA M. GREEN, FRANCISCO C. PRATS, and SHERIDAN K. SNEDDEN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

A. Background

Petitioner, Eli Lilly and Company ("Eli Lilly" or "Petitioner"), filed a Petition requesting *inter partes* review of claims 1–5 ("the challenged claims") of U.S. Patent No. 8,133,903 B2 ("the '903 patent"). Paper 1

("Pet."). Patent Owner, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center ("LA Biomed" or "Patent Owner"), filed a Corrected Patent Owner Preliminary Response. Paper 12 (Prelim. Resp.). We determined that the information presented in the Petition and the Preliminary Response demonstrated that there was a reasonable likelihood that Petitioner would prevail in challenging claims 1–5 as unpatentable under 35 U.S.C. § 102. Pursuant to 35 U.S.C. § 314, the Board instituted trial on October 23, 2014, as to the challenged claims of the '903 patent. Paper 14 ("Institution Decision" or "Dec. Inst.").

Patent Owner filed a Response (Paper 21, "PO Resp."), but did not file a motion to amend. Petitioner subsequently filed a Reply. Paper 26 ("Reply"). An oral hearing was held on June 16, 2015. The transcript of the hearing has been entered into the record. Paper 44. Patent Owner also filed a Motion for Observation on certain cross-examination testimony of Petitioner's declarant, Irwin Goldstein, M.D. (Paper 33, "Goldstein Obs."), as well as a Motion to Exclude Evidence (Paper 30).

We have jurisdiction under 35 U.S.C. § 6(c). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. Based on the record before us, we conclude that Petitioner has not demonstrated by a preponderance of the evidence that claims 1–5 of the '903 patent are anticipated.

B. Related Proceedings

According to the parties, the '903 patent is involved in the following copending case: *Los Angeles Biomedical Research Institute v. Eli Lilly & Co.*, No. 2:13-cv-08567-JAK-JCG (C.D. Cal.). Pet. 56; Paper 5.

In addition, Eli Lilly filed, concurrently with the instant Petition, an additional petition for *inter partes* review of claims 1–5 of U.S. Patent No. 8,133,903 B2 on different grounds, IPR2014-00752. A final decision is being entered in that case concurrently with the final decision in the instant case.

C. The '903 Patent (Ex. 1001)

The '903 patent issued on March 13, 2011, with Nestor F. Gonzalez-Cadavid and Jacob Rajfer as the listed co-inventors. Ex. 1001. The '903 patent relates to methods of treating fibrotic conditions with phosphodiesterase (PDE5) inhibitors (*e.g.* sildenafil). *Id.* at 1:20–27. The PDE5 inhibitor is administered at a dosage up to 1.5 mg/kg/day, wherein the maximum dosage is roughly equivalent to the dose ingested by men with an on-demand single 100 mg tablet. *Id.* at 45:7–12. Fibrotic conditions disclosed in the '903 patent include Peyronie's disease ("PD"), erectile dysfunction ("ED"), and arteriosclerosis. *Id.* at 1:29–2:46. The '903 patent discloses that the "[l]ong-term administration of nitrergic agents, such as . . . sildenafil . . . may be of use to reduce PD plaque size and collagen/fibroblast ratio and may reverse or prevent the further development of the fibrosis observed in PD, ED, arteriosclerosis and other fibrotic conditions." *Id.* at 3:8–14.

D. Challenged Claim

Petitioner challenges claims 1–5 of the '156 patent. Claim 1 is representative, and is reproduced below.

> 1. A method comprising:
> a) administering a cyclic guanosine 3′, 5′-monophosphate (cGMP) type 5 phosphodiesterase (PDE 5) inhibitor according

> to a continuous long-term regimen to an individual with at least one of a penile tunical fibrosis and corporal tissue fibrosis; and b) arresting or regressing the at least one of the penile tissue fibrosis and corporal tissue fibrosis, wherein the PDE-5 inhibitor is administered at a dosage up to 1.5 mg/kg/day for not less than 45 days.

E. Instituted Challenge

Claims	**Basis**	**Reference**
1–5	§ 102	Whitaker[1]

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1276–79 (Fed. Cir. 2015); Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,766 (Aug. 14, 2012). Claim terms also are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). "[A] claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to 'particularly point[ ] out and distinctly claim[ ] the subject matter which the patentee regards as his invention.'" *Innova/Pure*

[1] Whitaker et al. ("Whitaker"), Pub. No. WO 01/80860 A2, published Nov. 1, 2001 (Ex. 1086).

Water, Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1116 (Fed. Cir. 2004); *see also Pitney Bowes, Inc. v. Hewlett–Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999) ("The starting point for any claim construction must be the claims themselves."). Only terms which are in controversy need to be construed, and then only to the extent necessary to resolve the controversy. *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

1. "at a dosage up to 1.5 mg/kg/day for not less than 45 days"

Neither party has offered an express construction for this claim limitation, but instead the parties address the claim limitation "a continuous long-term regimen," which we also addressed in the Decision on Institution. *See* Pet. 14–15; PO Resp. 22–25; Reply 11–12; Dec. Inst. 8–10. The plain language of that limitation of claim 1, however, requires that a dosage up to 1.5 mg/kg/day be administered for at least 45 days. Also, administering a dosage up to 1.5 mg/kg/day for at least 45 days would, according to the language of the claim, meet the limitation of a "continuous, long-term regimen," as recited by claim 1.

We need not construe any other claim terms for purposes of this Decision.

B. Patentability

To prevail on its challenges to the patentability of claims, Petitioner must prove unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

1. Anticipation by Whitaker

Petitioner contends that Whitaker anticipates independent claim 1. Pet. 41–53. Petitioner sets forth claim charts indicating where each element

of the claim is allegedly taught by the reference (*id.* at 42–46), and relies, initially, on the Declaration of Dr. Goldstein (Ex. 1002). Patent Owner disagrees with Petitioner's assertions (PO Resp. 37–59), and relies on the Declaration of Trinity J. Bivalacqua, M.D. Ph.D. (Ex. 2023) as evidence that Whitaker does not anticipate the challenged claims. Petitioner then relies on an additional Declaration of Dr. Goldstein (Ex. 1121) in its Reply.

a. Whitaker (Ex. 1086)

Whitaker discloses methods of treating male erectile dysfunction involving the chronic administration of a PDE5 inhibitor at a dose of 1 mg/day to 10 mg/day. Ex. 1086, 4:13–23. Whitaker defines chronic as follows:

> The term "chronic or chronically" refers to the regular administration of the product in intervals unrelated to the onset of sexual activity. To receive the full benefit of the present invention, chronic administration generally refers to regular administration for an extended period, preferably daily for three or more days, and still more preferably daily as long as the patient suffers from erectile dysfunction (in the absence of therapy). The term "chronic" administration encompasses other regimens in addition to daily dosing. For example, chronic administration encompasses administration of a sustained release formulation that provides sufficient PDE5 inhibiter on a regular basis and unrelated to the onset of sexual activity. Contrary to acute or on-demand administration, chronic administration does not link the administration of the PDE5 inhibitor to the onset of sexual activity (e.g., one hour prior to intercourse).

Id. at 7:10–29.

Whitaker's Example 6 discloses the results of five clinical studies assessing the efficacy of daily oral dosing of a PDE5 inhibitor in males with erectile dysfunction. *Id.* at 34–37. According to Whitaker:

> One study was of eight weeks duration, and the other four studies were of twelve weeks duration. The Study Drug was administered "daily" to patients with male erectile dysfunction. "Erectile dysfunction (ED)" is defined as the persistent inability to attain and/or maintain an erection adequate to permit satisfactory sexual performance.

Id. at 34:17–24. There were four subgroups in the study, with the first subgroup taking the study drug less than 30% of the time during the study, the second subgroup taking the study drug 30% to 50% of the time during the study, the third subgroup taking the study drug 50% to 70% of the time during the study, and the fourth subgroup taking the study drug greater than 70% of the time during the study. *Id.* at 34:25–31. Whitaker teaches that the "Study Drug was administered in 5 mg and 10 mg doses, 'daily' and not more than once every 24 hours." *Id.* at 35:3–4. As taught by Whitaker, a better response was obtained with an increased frequency of dose. *Id.* at 36:1–4.

b. Analysis

Claim 1 is drawn a method of administering a PDE5 inhibitor, at a dosage up to 1.5 mg/kg/day for not less than 45 days.

As to the claim limitation that the PDE5 inhibitor is administered at least once a day for 45 days, Petitioner relies on Example 6 of Whitaker. Pet. 43–44. Specifically, Petitioner contends that the study reported in Example 6 of Whitaker lasted twelve weeks. *Id.* at 47.

Patent Owner contends that the chronic administration of Whitaker is not the same as the long-term regimen required by claim 1. PO Resp. 46. According to Patent Owner, although the studies in Example 6 of Whitaker "were ostensibly of eight or twelve weeks duration, *Whitaker* makes clear that the unidentified PDE-5 inhibitor . . . was not administered to the

subjects on each and every day." *Id.* at 48. Patent Owner contends that Whitaker in fact teaches that the "drug was administered as infrequently as 30% of the days and at most a little more than 70% of the days during the studies' duration, with no requirement that the days on which the drug was administered be consecutive [days]." *Id.*

Petitioner responds that Whitaker teaches daily treatment, and in fact, the title of the publication is "Daily treatment for erectile dysfunction using a PDE5 inhibitor." Reply 19. As for long-term treatment, Petitioner contends:

> While Example 6 shows that treatment for 8–12 weeks was contemplated, *Whitaker* expressly teaches a much longer treatment period (i.e., "daily **as long as the patient suffers from erectile dysfunction** (in the absence of therapy)"). Ex. 1086 at 7:17–19 (emphasis added). As both parties' experts agree, this duration would be at least months, if not longer. Ex. 1122 at 298:20–300:8; Ex. 1121 at ¶¶ 114–15, 119, 122. Thus, the prescription that would be written based on *Whitaker* would likewise be for long-term use, i.e., "as long as the patient suffers from erectile dysfunction." Ex. 1086 at 7:17–19; Ex. 1121 at ¶¶ 119, 122.

Id. at 21.

We agree with Patent Owner that Petitioner has not demonstrated that Whitaker anticipates claim 1 by a preponderance of the evidence. To anticipate, a prior art reference "must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)).

Petitioner does not rebut Patent Owner's argument that Example 6 of Whitaker, at most, teaches dosing about 70% of the days. Rather, Petitioner

relies on the title of Whitaker, which explicitly recites "daily dosing," along with the argument that Whitaker teaches that the treatment should continue as long as the patient suffers from erectile dysfunction, which would be months, if not longer. We are not persuaded.

Whitaker, although noting that the PDE5 inhibitor may be administered daily as long as the patient suffers from erectile dysfunction, specifically refers to regular administration for an extended period as being preferably daily for three or more days. Ex. 1086, 7:10–25. Whitaker also discloses that administering for as few as three days may effectively treat erectile dysfunction. *Id.* at 38:29–39:1. Although the ordinary artisan may have understood that patients may suffer from erectile dysfunction for months, if not longer, that, at best, is an obviousness argument. Thus, that argument is not sufficient to demonstrate, by a preponderance of the evidence, an inherent description of continuous administration for at least 45 days as required by claim 1, especially in view of Whitaker's teaching that a therapeutically effective extended period may be as short as three days. Moreover, in Example 6, when Whitaker actually administers for an extended period of time, at most, the study drug is taken daily approximately 70% of the time during the study. *Id.* at 34:25–31. Therefore, we determine that Petitioner has not demonstrated by a preponderance of the evidence that Whitaker anticipates claim 1.

2. Claims 2–5

Claims 2–5 are dependent on claim 1, and thus incorporate all of the limitations of that claim. Thus, the challenge of claims 2–5 as anticipated by Whitaker fails for the same reason as the anticipation challenge of claim 1 fails.

3. Conclusion

After considering Petitioner's and Patent Owner's positions, as well as their supporting evidence, we determine that Petitioner has not shown by a preponderance of the evidence that claims 1–5 are anticipated by Whitaker.

C. Patent Owner's Motion to Exclude Evidence (Paper 30)

Patent Owner seeks to exclude Petitioner's Exhibits 1103, 1106–1107, 1115–1116, 1118–1121, 1124, 1127, 1128–1130, 1131, 1135–1137, 1139–1140, 1142, 1144, and portions of Dr. Bivalacqua's deposition testimony (Ex. 1122). As we did not rely on any of those exhibits in this Decision, Patent Owner's Motion to Exclude is dismissed as moot.

D. Motion for Observation (Paper 33)

Patent Owner's observations are directed to the cross-examination testimony of Dr. Goldstein (Ex. 2108), who was cross-examined after Petitioner filed its Reply. Paper 33. As previously discussed, we did not rely on the Dr. Goldstein's Reply Declaration in this decision. Therefore, we need not consider Patent Owner's observations directed to the cross-examination testimony of Dr. Goldstein.

E. Objections to Demonstratives

Each of Petitioner (Paper 42) and Patent Owner (Paper 43) objected to the other's demonstratives. In view of those objections, we expunge the demonstratives from the record. Thus, Petitioner's demonstratives (Paper 41) and Patent Owner's demonstratives (Paper 40), are expunged.

III. CONCLUSION

Petitioner has not shown by a preponderance of the evidence that claims 1–5 are unpatentable under 35 U.S.C. § 102 as anticipated by Whitaker.

IV. ORDER

Accordingly, it is hereby:

ORDERED that Petitioner has not shown by a preponderance of the evidence that claims 1–5 of the ’903 patent are unpatentable;

FURTHER ORDERED that Petitioner’s Motion to Exclude is *dismissed* as moot;

FURTHER ORDERED that Papers 40 and 41 are expunged; and

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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