

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TARO PHARMACEUTICALS U.S.A., INC.,
Petitioner,

v.

APOTEX TECHNOLOGIES, INC.,
Patent Owner.

Case IPR2017-01446
Patent 7,049,328 B2

Before LORA M. GREEN, JEFFREY N. FREDMAN, and
ZHENYU YANG, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION
Request for Rehearing
37 C.F.R. § 42.71

Patent Owner, Apotex Technologies, Inc., filed a request for rehearing (Paper 11, “Req.”) of the Decision on Institution (Paper 7, “Dec.”) instituting *inter partes* review of claims 1, 2, 4–17, and 19 of U.S. Patent No. 7,049,328 B2 (Ex. 1001, “the ’328 patent”). In its request, Patent Owner contends the Decision misapprehended the law regarding inherency. Req. 2–13. The request for rehearing is *denied*.

ANALYSIS

When rehearing a decision on institution, the Board will review the decision for an abuse of discretion. 37 C.F.R. § 42.71(c). The applicable standard for a request for rehearing is set forth in 37 C.F.R. § 42.71(d), which provides in relevant part:

A party dissatisfied with a decision may file a request for rehearing, without prior authorization from the Board. The burden of showing a decision should be modified lies with the party challenging the decision. The request must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply.

Patent Owner “submits that the evidence of record fails to show that any of Hoffbrand 1998, Olivieri Abstract 1995, and Olivieri 1995 ‘unavoidably teaches’ the treatment of patients who *have* an iron overload condition of the heart or iron-induced cardiac disease.” Req. 2.

Hoffbrand 1998

Patent Owner specifically contends:

Hoffbrand 1998 never discloses that any patient has an iron overload condition of the heart or iron-induced cardiac disease on the basis of liver iron content. Instead, Hoffbrand 1998 states—as quoted by the Board—that the 10 patients had liver iron content “‘that has been associated with cardiac disease.’”

Req. 4. Appellants contend “although the Federal Circuit has made clear that inherency cannot be established based on ‘probabilities or possibilities,’ the Board based its conclusion on an ‘association’ between liver iron content and cardiac disease. An ‘association,’ however, does not meet the strict requirement of inevitability.” *Id.* at 5.

We agree with Patent Owner on the legal standard for inherency. As we acknowledged in our Decision, “[i]nherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *MEHL/Biophile Int’l. Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999).” Dec. 14.

However, we remain persuaded at this stage of the proceeding on the current factual record based on Hoffbrand 1998 and the Mehta Declaration, that Petitioner established a “reasonable likelihood” that Hoffbrand 1998 necessarily disclosed treatment of patients with “an iron overload condition of the heart” with a therapeutically effective amount of deferiprone. See Dec. 16–20; 35 U.S.C. § 314(a).

Patent Owner does not identify a definition of the phrase “iron overload condition of the heart” in the ’328 patent Specification that distinguishes the claimed patient population from Hoffbrand’s disclosure of “10 patients [that] had a liver iron content above 15.0 mg/g dry weight, ie, falling within the range that has been associated with cardiac disease.” Ex. 1007, 297. The reasonable understanding of Hoffbrand’s teaching of this association between liver iron content and cardiac disease is that all ten patients with the elevated iron levels also necessarily fell into the spectrum of having “an iron overload condition of the heart.”

Indeed, Patent Owner’s Declarants do not rebut Hoffbrand’s teaching that liver iron content above 15.0 mg/g identifies patients with cardiac disease, and, therefore, with “an iron overload condition of the heart.” Dr. Coates simply notes that Hoffbrand 1998 reports five treated “patients suffered fatal complications. . . . Four of the five reported fatalities resulted from congestive heart failure.” Ex. 2001 ¶ 37. *Cf.* Pennell Decl. Ex. 2003

¶ 37. That statement supports the position that Hoffbrand 1998 treated patients who inherently had an ultimately fatal “iron overload condition of the heart” with 75 mg of deferiprone, acknowledged by claim 15 of the ’328 patent as a therapeutically effective amount. Ex. 1007, 295; Ex. 1001, 28:33–37.

We recognize that Dr. Pennell stated that “a patient with a liver iron content above 15 mg/g dry weight is at risk of developing cardiac disease not that such liver iron content definitely establishes cardiac disease.” Ex. 2003 ¶¶ 50–51, citing Exhibits 2007, 2015, and 2016. The Exhibits cited by Dr. Pennell do not identify evidence showing a single patient with a liver iron content that exceeds 15.0 mg/g but failed to display an “iron overload condition of the heart.” See Ex. 2003 ¶ 51. Exhibit 2007 states “while whole liver iron levels >15 mg/g dry weight . . . have been shown to predict patients at highest risk of cardiac death, it is not known how these variables relate to cardiac iron deposition.” Ex. 2007, 1. No specific patient data is provided in Exhibit 2007 comparing liver iron levels of particular patients with “iron overload.” See *id.* Similarly, Exhibits 2015 and 2016 also do not identify any patients with elevated liver iron content >15 mg/g dry weight with normal cardiac iron levels.

Therefore, the evidence currently of record in Hoffbrand 1998, identifying ten patients as having liver iron levels associated with cardiac disease, provides factual support for finding a reasonable likelihood that these patients necessarily have an “iron overload condition of the heart.” See Ex. 1007, 297.

Olivieri Abstract 1995

Patent Owner contends “Olivieri Abstract 1995 never equates abnormal TRT values with ‘an iron overload condition of the heart’ or ‘iron-induced cardiac disease.’” Req. 6. Patent Owner contends:

the Board nonetheless instituted trial on the basis of inherent anticipation thereby committing legal error in at least three respects. *First*, although the Federal Circuit has made clear that inherency cannot be established based on “probabilities or possibilities,” the Board improperly based its conclusion on the notion that abnormal TRT values indicate high cardiac iron, which in turn indicates cardiac disease.

Id. at 7. Patent Owner contends: “*Second*, the Board committed legal error when it based its assumptions on unsubstantiated testimony from Dr. Mehta.” *Id.* at 8. Patent Owner contends “Dr. Mehta’s statement that ‘lower TRT values indicate cardiac disease due to iron overload.’ (see Ex. 1002 at ¶ 75) is not based on any underlying fact or data, but instead is mere conjecture.” *Id.* at 8.

Patent Owner contends also:

Third, the Board appeared to improperly shift the burden of proof . . . The proper focus is not whether the Patent Owner, and its Declarants, provided evidence rebutting that Olivieri Abstract 1995 taught patients having an iron overload condition of the heart (which, to be clear Patent Owner did (see Preliminary Response at 43–44)), but whether Petitioner came forth with evidence sufficient to demonstrate this limitation was disclosed in Olivieri Abstract 1995.

Req. 9.

We address these arguments *seriatim*. Regarding the first argument, we found “Olivieri Abstract 1995 inherently anticipates even under a requirement ‘that the claimed method have been actually performed.’

Montgomery, 677 F.3d at 1382, because deferiprone was administered in amounts claimed by the '328 patent as 'therapeutically effective' to patients with evidence of iron overload of the heart. Ex. 1010." Dec. 24.

No specific degree of "iron overload" of the heart is required by the claims of the '328 patent. Therefore, for purposes of institution, any excess amount of iron subject to treatment in order to reduce the iron levels is reasonably interpreted as a degree of "an iron overload condition of the heart." As discussed in the Decision, the Olivieri Abstract 1995 determined that treatment with deferiprone reduced iron levels in patients with thalassemia major. See Dec. 22, citing Ex. 1010. Thus, because Olivieri Abstract 1995 is reasonably understood as demonstrating reduction in cardiac iron levels in patients being treated to reduce cardiac iron levels, Olivieri Abstract 1995 necessarily treats "an iron overload condition of the heart."

Regarding the second argument, Dr. Mehta relied upon specific facts within the Olivieri Abstract 1995 itself to support the conclusion that "lower TRT values indicate cardiac disease due to iron overload. Ex. 1010 (Olivieri Abstract 1995)." Ex. 1002 ¶ 75. In particular, Olivieri Abstract 1995 states "MRI demonstrates changes consistent with reduction in cardiac iron in L1 [deferiprone]-treated pts, in who baseline T2 relaxation time (TRT of 23.9 ± 6.4 msec (normal >32) has increased to 32.4 ± 9.3 msec." Ex. 1010. Olivieri Abstract 1995's identification of the value of "32" as normal for TRT levels with lower values such as " 23.9 ± 6.4 " as associated with elevated cardiac iron levels that require treatment with deferiprone, provides factual support for Dr. Mehta's conclusion that patients with these lower TRT

values inherently have “an iron overload condition of the heart.” See Ex. 1002 ¶ 75.

Regarding the third argument, we do not agree that we placed the burden of production on Patent Owner. As discussed in *Dynamic Drinkware* there are two distinct burdens of proof: a burden of persuasion and a burden of production. . . . the burden of persuasion is on the petitioner to prove “unpatentability by a preponderance of the evidence,” 35 U.S.C. § 316(e), and that burden never shifts to the patentee. . . . A second and distinct burden, the burden of production, or the burden of going forward with evidence, is a shifting burden, “the allocation of which depends on where in the process of trial the issue arises.” [citing *Tech. Licensing Corp. v. Videotek, Inc.* 545 F.3d 1316, 1326–27 (Fed. Cir. 2008)].

Dynamic Drinkware, LLC v. National Graphics, Inc., 800 F.3d 1375, 1378–79 (Fed. Cir. 2015). In the instant case, our Decision to Institute found Petitioner has satisfied both the burden of production to show that Olivieri Abstract 1995 is anticipating prior art and a reasonable likelihood to satisfy Petitioner’s burden of proof at institution to demonstrate that Olivieri Abstract 1995, as supported by the Mehta Declaration, supports a reasonable likelihood of claim invalidity.

As the Decision notes, we found that the evidence presented by Petitioner provided a reasonable likelihood of anticipation by the Olivieri Abstract 1995. See Dec. 24. We then addressed whether Patent Owner had provided evidence, that when considered with Petitioner’s evidence, was sufficient to conclude that Olivieri Abstract 1995 did not anticipate the claims. We found that Patent Owner’s experts provided no particularized facts demonstrating that the evidence regarding the specific treatment of specific patients with 75 mg of deferiprone that result in reduction of cardiac

iron levels in the Olivieri Abstract 1995 was incorrect. *See* Dec. 24.

“[T]estimonial evidence will be viewed in the light most favorable to the petitioner solely for purposes of deciding whether to institute an inter partes review.” 37 C.F.R. § 42.108(c).

Therefore, the evidence currently of record in Olivieri Abstract 1995, identifying thalassemia major patients as having TRT levels associated with increased cardiac iron levels who were treated with 75 mg of deferiprone resulting in normal TRT levels, provides support for concluding that Petitioner had established a reasonable likelihood that these patients necessarily have an “iron overload condition of the heart.” *See* Ex. 1010.

Olivieri 1995

Patent Owner contends

Olivieri 1995 merely discloses the treatment of ten patients who had hepatic iron stores at levels “associated with an increased risk” of cardiac disease, but Olivieri 1995 never characterized any patient as actually having “an iron overload condition of the heart” or “iron-induced cardiac disease,” a disclosure that neither Petitioner nor Dr. Mehta relied upon in alleging inherent anticipation. The Board nonetheless instituted trial based on inherent anticipation, and in doing so committed legal error. Patients having an increased **risk** of cardiac disease does not and cannot establish the required **inevitability** that the patients in Olivieri 1995 **had cardiac disease**.

Req. 11.

We remain unpersuaded by these arguments for the reasons given in the Decision. *See* Dec. 30–31. In particular, Patent Owner does not identify a definition of the phrase “iron overload condition of the heart” in the ’328 patent Specification that distinguishes the claimed patient population from Olivieri 1995’s disclosure of “10 patients in whom deferoxamine had failed

to reduce hepatic iron stores to a level below 80 μmol of iron per gram (levels associated with an increased risk of cardiac disease and early death).” Ex. 1012, 921. The reasonable understanding of Olivieri 1995’s teaching of this association between hepatic iron stores and cardiac disease is that all ten patients with the elevated iron levels also necessarily fell into the spectrum of having “an iron overload condition of the heart.” See Dec. 31.

Obviousness

Patent Owner contends: “For the same reasons as discussed above, the Petitioner has not made a threshold showing that each of these three references teach patients having an iron overload condition of the heart or iron-induced cardiac disease, and the Board improperly applied the inherency standard when it found otherwise.” Req. 13.

We find this argument unpersuasive for the reasons given above.

Summary

As noted in the decision on institution (Dec. 2), the standard for instituting an *inter partes* review is set forth in 35 U.S.C. § 314(a), which provides:

THRESHOLD – The Director may not authorize an *inter partes* review to be instituted unless the Director determines that the information presented in the petition filed under section 311 and any response filed under section 313 shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.

As also noted in the decision on institution, we have considered both the Petition and Patent Owner Preliminary Response, and determined that the information presented in the Petition demonstrates that there is a reasonable likelihood that Petitioner would prevail with respect to the

challenged claims. Dec. 2. Therefore, we applied the correct threshold standard for instituting the *inter partes* review.

As such, Patent Owner has not shown that we misapprehended or overlooked any matters in instituting *inter partes* review. See 37 C.F.R. § 42.71(d). Thus, for the forgoing reasons, Patent Owner has not shown that the Board abused its discretion in instituting this *inter partes* review.

CONCLUSION

Patent Owner's request for rehearing is *denied*.

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