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Paper 10
Entered: August 25, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PRAXAIR DISTRIBUTION, INC. and NOxBOX LIMITED,
Petitioner,
v.
INO THERAPEUTICS LLC,
Patent Owner.

Case IPR2016-00781
Patent 8,846,112 B2

Before LORA M. GREEN, TINA E. HULSE, and
ROBERT A. POLLOCK, *Administrative Patent Judges.*

POLLOCK, *Administrative Patent Judge*.

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

I. INTRODUCTION

Petitioner, Praxair Distribution, Inc. ("Praxair") and NOxBOX Limited ("NOxBOX"), filed a Petition (Paper 4; "Pet.") to institute an *inter partes* review of claims 1–19 of U.S. Patent No. 8,846,112 B2 (Ex. 1001; "the '112 patent").[1] Patent Owner, Mallinckrodt Hospital Products IP Ltd.,[2] filed a Patent Owner Preliminary Response arguing, *inter alia*, that Petitioner is estopped from requesting or maintaining this IPR under 35 U.S.C. § 315(e)(1), and that the Board should exercise its discretion to deny this Petition under 35 U.S.C. § 325(d). Paper 8 ("Prelim. Resp."), 15–37.

We have jurisdiction under 35 U.S.C. § 314. For the reasons provided below, we deny the Petition for an *inter partes* review under 35 U.S.C. §§ 315(e)(1) and 325(d).

II. BACKGROUND

A. The '112 Patent

The '112 patent issued on September 30, 2014, from a series of continuation and divisional applications beginning with application No. 12/494,598 filed on June 30, 2009. Ex. 1001. The '112 patent is broadly directed to "methods of distributing a pharmaceutical product comprising nitric oxide gas" (*id.* Abstract) and discloses that nitric oxide is a lung-specific vasodilator that significantly improves blood oxygenation and reduces the need for extracorporeal oxygenation. *Id.* at 3:36–45, 7:1–29.

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[1] Praxair further identifies Praxair, Inc. as a real party-in-interest. Pet. 8.

[2] Patent Owner further identifies "INO Therapeutics LLC, Mallinckrodt Hospital Products, Inc., and Mallinckrodt PLC, affiliates of Mallinckrodt Hospital Products IP Ltd." as real parties-in-interest. Paper 6, 1.

INOmax® is an FDA-approved blend of nitric oxide and nitrogen, which may be administered in conjunction with ventilary support for iNO (inhaled nitric oxide) therapy. *Id*. at 1:20–25, 3:34–36, 3:57–62. The product is approved "for treatment of . . . term and near-term (>34 weeks gestation) neonates having hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension, a condition also known as persistent pulmonary hypertension in the newborn (PPHN)." *Id*. at 6:34–40. iNO has also been used for a variety of other conditions, where it generally "acts by preventing or treating reversible pulmonary vasoconstriction, reducing pulmonary arterial pressure and improving pulmonary gas exchange." *Id*. at 6:40–52.

Example 1 of the Specification discusses the conduct and results of the INOT22 Study, in which children undergoing cardiac catheterization were administered oxygen, oxygen in conjunction with iNO, or iNO alone. *Id*. at 9:35–10:27. The Specification states that "[i]dentifying patients with pre-existing LVD [left ventricular dysfunction] is known to those skilled in the medicinal arts, and such techniques for example may include assessment of clinical signs and symptoms of heart failure, or echocardiography diagnostic screening." *Id*. at 5:15–19. During the INOT22 study, patients with pre-existing LVD experienced an increased rate of serious adverse events (SAEs) including pulmonary edema. *See, e.g.*, *id*. at 9:47–51, 14:17–25. In an effort to minimize the risk of adverse events, the INOT22 protocol was amended to exclude patients with an elevated pulmonary capillary wedge pressure (PCWP). *See id*. at 14:17–25. PCWP is a measure of left atrial pressure that may be used to diagnose LVD. *Id*. at 5:20–28. The Specification states, for example:

> The upper limit of normal PCWP in children is 10-12 mm Hg and 15 mm Hg in adults. In INOT22, a baseline PCWP value was not

> included as exclusion criteria. However, after the surprising and unexpected identification of SAEs in the early tested patients, it was determined that patients with pre-existing LVD had an increased risk of experiencing an AE or SAE upon administration (e.g., worsening of left ventricular function due to the increased flow of blood through the lungs). Accordingly, the protocol for INOT22 was thereafter amended to exclude patients with a baseline PCWP greater than 20 mm Hg after one patient experienced acute circulatory collapse and died during the study. The value "20 mm Hg" was selected to avoid enrollment of a pediatric population with LVD such that they would be most likely at-risk for these SAEs.

Id. at 12:47–61. In light of the above results indicating that iNO therapy may be detrimental to patients with pre-existing LVD, the Specification proposes amending the INOmax® prescribing information to include a precaution for patients with LVD. *Id*. at 9:51–53.

B. Prior Adjudication of All Claims

Praxair previously requested *inter partes* review of claims 1–19 of the '112 patent in IPR2015-00529. In our Final Written Decision in that proceeding, we determined that Praxiar had demonstrated by a preponderance of the evidence that claims 1–8 and 10–19 of the '112 patent were unpatentable, but determined that Praxair had not proven by a preponderance of the evidence that claim 9 was unpatentable. *Praxair Distribution, Inc. v. Mallinckrodt Hospital Prods. IP Ltd.*, Case IPR2015-00529, slip op. at 39–42, 46 (July 7, 2016) (Paper 53) ("*Praxair I*").[3]

[3] Praxair also requested, and the Board denied, institution of *inter partes* review of four related patents that share the same specification as the '112 patent. *Praxair Distribution, Inc. v. Mallinckrodt Hospital Prods. IP Ltd.*, Case IPR2015-00522, -0524, -00525, -00526, slip op. at 25 (July 29, 2015) (Paper 53).

C. Illustrative Claim and "Providing . . . Information" Step

The independent claims at issue, claims 1, 7, 12, and 14 of the '112 patent, involve "supplying [a] cylinder containing compressed nitric oxide gas to a medical provider" in conjunction with a "providing . . . information" step, generally related to the finding that in patients with pre-existing left ventricular dysfunction, inhaled nitric oxide may increase pulmonary capillary wedge pressure (PCWP) leading to pulmonary edema, such that iNO is contraindicated in this patient subpopulation. The "providing . . . information" step of illustrative claim 1 (formatted for clarity), is set forth below in italics:

> 1. A method of providing pharmaceutically acceptable nitric oxide gas, the method comprising:
> obtaining a cylinder containing compressed nitric oxide gas in the form of a gaseous blend of nitric oxide and nitrogen:
> supplying the cylinder containing compressed nitric oxide gas to a medical provider responsible for treating neonates who have hypoxic respiratory failure, including some who do not have left ventricular dysfunction;
> *providing to the medical provider*
> *(i) information that a recommended dose of inhaled nitric oxide gas for treatment of neonates with hypoxic respiratory failure is 20 ppm nitric oxide and*
> *(ii) information that, in patients with pre-existing left ventricular dysfunction, inhaled nitric oxide may increase pulmonary capillary wedge pressure (PCWP), leading to pulmonary edema,*
> *the information of (ii) being sufficient to cause a medical provider considering inhaled nitric oxide treatment for a plurality of neonatal patients who (a) are suffering from a condition for which inhaled nitric oxide is indicated, and (b) have pre-existing left ventricular dysfunction, to elect to avoid treating one or more of the plurality of patients with inhaled nitric oxide in order to avoid putting the one or more patients at risk of pulmonary edema.*

In construing the claims of the '112 patent in IPR2015-00529, we determined that the "information" provided in this, and similarly-worded claim steps in other claims, constituted printed matter and, therefore, accorded the term no patentable weight with respect to claims 1–8 and 10–19. *See Praxair I*, 15–21.[4] In the matter before us, Petitioner states that "the instant Petition is crafted under the assumption that all of the claim elements in the '112 patent should be given patentable weight" (Pet. 9), but that "[i]f [*Praxair I*] does not give the 'providing information' limitations patentable weight, then . . . the Board need not consider the present petition except in the eventuality of Federal Circuit reversal" (*id.* at 12; *see id.* at 1, n.1). Consistent with this focus on the "providing . . . information" limitation, Petitioner asserts that the challenged claims are unpatentable in light of INOmax label[5] (the primary reference asserted in IPR2015-00529) and two "recently discovered" references, Greenough[6] and Jaypee,[7] which allegedly disclose the provided "information." *See e.g.*, Pet. 13–14, 15, 22–25, 33–34.

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[4] We likewise determined that the similar language of independent claim 7, cast as "providing . . . a recommendation," was also entitled to no patentable weight. *Id.* at 21–22; *see id.* at 21, n.11. For the purpose of this Decision, we consider collectively the "providing" limitations of claims 1–8 and 10–19.

[5] Center for Drug Evaluation and Research, Application Number: NDA 20845, INOmaxTM, Final Printed Labeling, *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/99/20845_INOmax_prntlbl.pdf (August 9, 2000). ("INOmax label"). Ex. 1010.

[6] NEONATAL RESPIRATORY DISORDERS, 149, 183–87, 392 (Anne Greenough & Anthony D. Milner eds., 2nd ed. 2003) ("Greenough"). Ex. 1006.

[7] Praveen Khilnani, PEDIATRIC & NEONATAL MECHANICAL VENTILATION 148–58 (Jaypee Brothers Medical Publishers, Ltd., New Dehli, 2006) ("Jaypee"). Ex. 1007.

We consider below whether Petitioner is estopped from requesting this IPR under 35 U.S.C. § 315(e)(1) and, separately, whether the Board should exercise its discretion to deny this Petition under 35 U.S.C. § 325(d).

III. ANALYSIS – 35 U.S.C. § 315(e)(1)

Once a Petitioner has obtained a final written decision, that Petitioner may not request or maintain subsequent proceedings on a ground that it "reasonably could have raised" during the prior proceeding. *See Dell Inc. v. Elecs. and Telecomms. Research Inst.*, IPR2015-00549, slip. op. 4–6 (PTAB Mar. 26, 2015) (Paper 10) (representative). Specifically, section 315(e)(1) of the Patent Statute provides:

> (e) Estoppel. —
>
> (1) Proceedings before the office.—The petitioner in an inter partes review of a claim in a patent under this chapter that results in a final written decision under section 318(a), or the real party in interest or privy of the petitioner, may not request or maintain a proceeding before the Office with respect to that claim on any ground that the petitioner raised or reasonably could have raised during that inter partes review.

35 U.S.C. § 315(e)(1); *see* 37 C.F.R. § 42.73(d).

As in this proceeding, Praxair challenged claims 1–19 of the '112 patent in IPR2015-00529. On July 7, 2016, that earlier proceeding resulted in a final written decision, pursuant to 35 U.S.C. § 318(a).

The legislative history of the America Invents Act broadly describes grounds that "reasonably could have been raised" as encompassing "prior art which a skilled searcher conducting a diligent search reasonably could have been expected to discover." 157 Cong. Rec. S1375 (daily ed. Mar. 8, 2011) (statement of Sen. Kyl); *see id*. at S1376 (statement of Sen. Kyl) ("This [estoppel] effectively bars

such a party or his real parties in interest or privies from later using inter partes review . . . against the same patent, since the only issues that can be raised in an inter partes review . . . are those that could have been raised in [an] earlier post-grant or inter partes review."); 157 Cong. Rec. S952 (daily ed. Feb. 28, 2011) (statement of Sen. Grassley) ("It also would include a strengthened estoppel standard to prevent petitioners from raising in a subsequent challenge the same patent issues that were raised or reasonably could have been raised in a prior challenge.").

A. Whether Praxair Reasonably Could Have Raised Greenough and Jaypee During the Earlier Proceeding and Is, Therefore, Estopped Under 35 U.S.C. § 315(e)

Petitioner describes Greenough as "a textbook on neonatal respiratory disorders, including indications and contraindications for iNO treatment," including "an entire chapter dedicated to the treatment of persistent pulmonary hypertension of the newborn ("PPHN")." Pet. 22–23. Petitioner similarly describes Jaypee as "a textbook on pediatric and neonatal mechanical ventilation that reviews pediatric conditions, including pulmonary hypertension and PPHN," and encompasses "an entire chapter on iNO." *Id.* at 23–24. Despite their evident relevance to the subject matter of the '112 patent, Petitioner contends that "[d]espite conducting diligent searches, Praxair did not find the *Greenough* or *Jaypee* references prior to filing the first set of IPRs," including IPR2015-00529. *Id.* at 15. We infer that these references came to Petitioner's attention some time after they were cited by the Examiner during the prosecution of one or more applications related to the '112 patent. *See* Pet. 15; Prelim. Resp. 18, 35; Ex. 2014, 3, 5, 21–23 (April 29, 2015, Office Action, Notice of References Cited, and

Examiner's Search Report for Application No. 14/454,373, each citing Greenough and Jaypee).

As evidence of diligence in searching the prior art, Petitioner submits Exhibit 1009, an "Exemplary List of Search Results from Cardinal Intellectual Property, Inc." Pet. 15. But, as Patent Owner points out, Petitioner's assertion that it did not find Greenough or Jaypee "[d]espite conducting diligent searches" is predicated on a single search report by an unidentified searcher of indeterminate skill and experience listing a mere fifteen "exemplary" search results. *See* Prelim. Resp. 18–19; Pet. 15; Ex. 1009. Petitioner does not, as Patent Owner points out, "identify the actual searcher, his or her skill level and experience in the field, [] why he or she searched using certain keywords and keyword combinations," or explain whether either Greenough or Jaypee were encompassed by the initial search results but not selected for the exemplary list. Prelim. Resp. 19. On the record before us, we, therefore, find scant evidence that Praxair engaged "a skilled searcher conducting a diligent search" as contemplated in the legislative history. *See* 157 Cong. Rec. S1375.

Also at odds with Petitioner's assertion of diligence is Petitioner's contention that "a person of skill in the art would have been seeking out [Greenough and Jaypee] when trying to ascertain the collective academic thinking regarding iNO therapy as of the [earliest priority date]" of the '112 patent. Pet. 26. In addition, the testimony of Petitioner's technical expert, Dr. Lawson, evidences that the newly-asserted references are not obscure texts unlikely to be discovered upon a reasonably diligent search of the relevant prior art. In particular, Dr. Lawson states that:

> A person of skill in the art interested in iNO treatment would have referred to the INOmax Label, *Greenough* and *Jaypee* as they are all

> part of a collected literature regarding treatment of patients with iNO. Anne Greenough, the author of *Greenough*, is a thought leader in this area. Moreover, the authors of *Greenough* and *Jaypee* are familiar with each other's works; for example, *Jaypee* cites other articles authored by Anne Greenough.

Ex. 1002 ¶ 51. Consistent with Dr. Lawson's testimony, Petitioner admits that "other articles by the author of *Greenough* were cited during prosecution" (Pet. 24, n.11), whereas Patent Owner provides evidence that Greenough is catalogued and accessible "at dozens of major libraries in the United States, including the Library of Congress, the National Library of Medicine, and the Harvard University Library," and that both textbooks are readily identified by searching Google Books using keywords from the '112 Patent specification. Prelim. Resp. 17–18 (citing Exs. 2003, 2008-2013).

On the record before us, we are not persuaded that Petitioner has demonstrated that a skilled searcher conducting a diligent search would not have expected to discover Greenough and Jaypee. Accordingly, we determine that Petitioner Praxair reasonably could have raised the grounds asserted here in IPR2015-00529. And, because Praxair previously challenged claims 1–19 of the '112 Patent in IPR2015-00529, which resulted in a final decision under § 318(a), it is now estopped under 35 U.S.C. § 315(e)(1) from requesting or maintaining the current proceeding before the Office with respect to those claims. *See Westlake Servs., LLC v. Credit Acceptance Corp.*, No. CBM2014-00176, slip. op. 3–5 (PTAB May 14, 2015) (precedential) (applying estoppel provision to all claims subject to a final written decision).

B. Whether Praxair's Foreign Subsidiary, NOxBOX, is Estopped Under 35 U.S.C. § 315(e)

As noted above, the estoppel provision of 35 U.S.C. § 315(e) expressly applies not only to a named petitioner, but to "a real party in interest or privy of the petitioner." Our rules similarly provide that:

> A petitioner, *or the real party in interest or privy of the petitioner*, is estopped in the Office from requesting or maintaining a proceeding with respect to a claim for which it has obtained a final written decision on patentability in an *inter partes* review . . . on any ground that the petitioner raised or reasonably could have raised during the trial.

37 C.F.R. § 42.73(d)(1) (emphasis added).

"[A]t a general level, the 'real party-in-interest' is the party that desires review of the patent" whereas, "[t]he notion of 'privity' is more expansive, encompassing parties that do not necessarily need to be identified in the petition as a 'real party-in-interest.'" Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,759 (Aug. 14, 2012). "Privity is essentially a shorthand statement that collateral estoppel is to be applied in a given case . . . . The concept refers to a relationship between the party to be estopped and the unsuccessful party in the prior litigation which is sufficiently close so as to justify application of the doctrine of collateral estoppel." *Id.* (quoting 154 Cong. Rec. S9987 (daily ed. Sept. 27, 2008) (statement of Sen. Kyl)). In determining whether privity exists, "[t]he emphasis is not on the concept of identity of parties, but on the practical situation." *Id.*

Petitioner discloses that NOxBOX, a UK company, "is an iNO delivery device manufacturer and was recently acquired by Praxair, Inc., to complement Praxair Distribution, Inc. which is the manufacture of iNO drug to be marketed under the brand Noxivent™." Pet. 8, 17.

We agree with Patent Owner. NOxBox is a privy of Praxair, Inc., a real party-in-interest in IPR2015-00529 (as well as in the instant case). *See* Pet. 8; IPR2015-00529, Paper 1 at 6. Under the facts before us, we determine that NOxBOX is estopped under § 315(e) from participating in this proceeding and, accordingly, deny the instant Petition for an *inter partes* review.

IV. ANALYSIS – 35 U.S.C. § 325(d)

Patent Owner argues that the Board should exercise its discretion under 35 U.S.C. § 325(d) to deny the instant Petition because Praxair "advances substantially the same arguments it presented in the prior -00529 proceeding," "was, or should have been, aware of the newly asserted *Greenough* and *Jaypee* references when it filed its first petition," and "is unfairly using the previous IPR proceeding as a roadmap to remedy the deficiencies in its first petition." Prelim. Resp. 2, 21–37. Petitioner, in contrast, contends that "the Board should institute trial in light of the discretion permitted by 35 U.S.C. § 325(d)" because the instant Petition "is directed to *entirely new* art and arguments, including specific recitations of information" recited in the claimed "providing" steps. Pet. 1; *see id.* at 12–14.

We do not find Petitioner's arguments persuasive. Although Petitioner now relies on Greenough and Jaypee, its underlying argument—that the prior art taught or suggested the exclusion of neonates with LVD from iNO treatment—is essentially the same as that raised in IPR2015-00529. Whereas Petitioner characterizes its present art and arguments as "explicitly contraindicat[ing] patients with LVD from iNO treatment" and "substantially different from those previously considered by the Office because all of the references unquestionably relate to *neonates*" (Pet. 13–14), the earlier Petition asserted that "*Bernasconi* discloses that

iNO can lead to pulmonary edema in neonates with LVD," such that one of ordinary skill in the art would "look to *Bernasconi* . . . to understand the additional contraindications and potential adverse reactions, beyond those approved by the FDA, relating to iNO therapy." *Praxair Distribution, Inc. v. Mallinckrodt Hospital Prods. IP Ltd.*, Case IPR2015-00529, Paper 1 at 11, 19 (July 5, 2015).

Petitioner's "*entirely new*" argument, thus, appears to be that Greenough and Jaypee expressly state that which one of ordinary skill in the art would have understood from the art cited in IPR2015-00529. Further, given that Petitioner raises Greenough and Jaypee as allegedly disclosing the same "information" that we previously accorded no patentable weight in the "providing" limitations of claims 1–8 and 10–19, Petitioner's argument with respect to these claims is effectively unchanged as compared to the prior IPR proceeding. *See* section II(B) and (C), *supra*.

Accordingly, because, Petitioner now advances the same or substantially the same arguments it presented in IPR2015-00529 and because, as discussed above, it should have been aware of the newly-cited Greenough and Jaypee references when it filed the earlier Petition, we exercise our discretion under § 325(d) to deny the instant Petition with respect to all challenged claims.

V. ORDER

For the reasons given, it is

ORDERED that Praxair Distribution Inc., and NOxBOX Limited are estopped under § 315(e) from participating in this proceeding and, accordingly, the Petition for an *inter partes* review is denied; and

FURTHER ORDERED that the Petition is denied under § 325(d) with respect to all claims.

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