Trials@uspto.gov
Tel: 571-272-7822

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.

---

[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.*

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.