IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT TRIAL AND APPEAL BOARD

PRAXAIR DISTRIBUTION, INC. AND NOxBOX LIMITED
Petitioner

v.

MALLINCKRODT HOSPITAL PRODUCTS IP LTD., AND INO THERAPEUTICS, INC. d/b/a IKARIA, INC.
Patent Owner

DECLARATION OF DR. EDWARD LAWSON
IN SUPPORT OF PETITION FOR
***INTER PARTES* REVIEW OF U.S. PATENT NO. 8,431,163**

I, Dr. Edward Lawson, declare that:

QUALIFICATIONS

1. I am a Professor Emeritus in Pediatrics at Johns Hopkins University. I have a Bachelor's Degree from Harvard University and a Medical Degree from Northwestern University Medical School. I interned in Pediatrics and did a neonatology fellowship at Children's Hospital Medical Center, Boston Hospital for Women and Beth Israel Hospital in Boston, MA. I was a Research Fellow in pediatrics at Harvard Medical School.

2. I have practiced neonatology since 1978. During my practice, I held various leadership and research positions. I have been active in managing premature, full-term and older infants with hypoxic respiratory failure of many different etiologies. I have extensive clinical experience with the utilization of nitric oxide therapy for relief of persistent pulmonary hypertension, BPD and other disorders.

3. I was the Chair of the American Lung Association/American Thoracic Society Research Committee. I am also an active member of many NIH study sections where grants related to neonatal pulmonary research have been decided.

4. I am currently the Editor-in-Chief for the Journal of Perinatology (the Official Journal of the Section on Neonatal Perinatal Medicine of the American

Academy of Pediatrics). I also have experience as an editor for the Fetal and Neonatal section of the Journal of Pediatrics.

5. I joined the Johns Hopkins faculty in 1999. At Johns Hopkins I have served as the Director of the Sutland/Pakula Family Newborn Critical Care Center, in the Division of Neonatal and Perinatal Medicine. I also served as the Vice Chair of the Department of Pediatrics at Hopkins Children's Center.

6. A copy of my curriculum vitae is attached as Exhibit 1003.

7. I am not an employee of Praxair Distribution, Inc.; Praxair, Inc., NOxBOX Limited or any affiliated company. Rather, I have been engaged in the present matter to provide my independent analysis of the issues raised in the above-mentioned *inter partes* review of U.S. Patent No. 8,431,163 ("the '163 Patent") Ex. 1001. I have received no compensation for this declaration beyond my normal hourly compensation of $425 for time actually spent studying the matter, and I will not receive any added compensation based on the outcome of any proceeding relating to the '163 Patent.

8. Based upon my extensive knowledge and years of experience in this field, I have an understanding of how inhaled NO was being used for medical treatment on or before June 30, 2009, as well as the risks and contraindications associated with its use. My analysis on this matter, as set forth below, is based on

my personal experience and what was known, and in fact, considered to be standard by one skilled in the art prior to June 30, 2009.

9. I have reviewed and am familiar with the '163 Patent. (Ex. 1001). Additionally, I have reviewed the following documents: (1) Ex. 1006, A. Greenough & A. D. Miller, *Neonatal Respiratory Disorders* 149, 183–87, 392 (2nd ed. 2003) ("*Greenough*"); (2) Ex. 1007, Jaypee, *Pediatric & Neonatal Mechanical Ventilation* 148–58 (Praveen Khilnani ed., 1st ed. 2006) ("*Jaypee*"); and (3) Ex. 1008, A. Widlitz *et al*, Pulmonary arterial hypertension in children, *European Respiratory Journal*, (January 2003) ("*Widlitz*"). I was already familiar with the concepts and physiology of iNO and its uses. I have also reviewed the documents cited elsewhere herein, as well as any documents cited in the declarations I have submitted or will submit in other *inter partes* review petitions arising out of my engagement in this matter. I have also reviewed the prosecution file history for the '163 Patent, as well as the other patents on which I have opined in this engagement, particularly the declarations submitted during prosecution. Based on the references and my experience and background, I do not agree that INOT22 study provides evidence that the claims are patentable; nor do I agree that the claim elements were not known. Specifically, as discussed below, the allegedly unknown aspects of the INOT22 study were clearly disclosed by, for example, *Greenough* and *Jaypee* prior to June 30, 2009.

10. My opinions, explained below, are based on my education, experience, and background in the field discussed above as well as my review of the references cited above.

BACKGROUND KNOWLEDGE OF ONE OF SKILL IN THE ART BEFORE THE '163 PATENT

11. The '163 Patent is entitled "Methods of Reducing the Risk of Occurrence of Pulmonary Edema Associated with Inhaled Nitric Oxide." The '163 Patent provides contraindications for treatment of neonates with inhaled NO. Specifically the '163 Patent provides a pre-screening protocol to determine whether a patient is at risk of an adverse event upon treatment with NO, such as pulmonary edema.[1] *See* Ex. 1001 at Abstract, 1:47-60. It essentially provides that if the patient demonstrates characteristics suggesting that he or she is at risk of harm, then the patient should not be treated with NO. *Id.* The evaluation includes a determination that patients who have left ventricular dysfunction should be excluded from treatment. *Id.* Claim 1 is representative:

> A method of reducing the risk of occurrence of pulmonary edema associated with a medical treatment comprising inhalation of 20 ppm nitric oxide gas, said method comprising:
>
> (a) performing echocardiography to identify a term or near-term neonate patient in need of 20 ppm inhaled nitric oxide treatment for hypoxic

[1] Pulmonary edema is a buildup of fluid in the lungs.

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