CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20845

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-845

DEC 23 [illegible]

INO Therapeutics, Inc.
Attention: Richard N. Williams, Ph.D.
54 Old Highway 22
Clinton, NJ 08809

Dear Dr. Williams:

Please refer to your new drug application (NDA) dated June 16, 1997, withdrawn on September 17, 1997 and resubmitted on May 26, 1999, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for INOmax (nitric oxide) 100 and 800 ppm for Inhalation.

We acknowledge receipt of your submissions dated December 8, 1999 (two).

This new drug application provides for the use of INOmax (nitric oxide) 100 and 800 ppm for Inhalation , in conjunction with ventilatory support and other appropriate agents, in the treatment of term and near-term (> 34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension, where it improves oxygenation and reduces the need for extracorporeal membrane oxygenation.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert submitted, immediate container and carton labels included in your December 8, 1999 submission). Accordingly, the application is approved effective on the date of this letter.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). We note that you have fulfilled the pediatric study requirement at this time.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Ms. Zelda McDonald
Regulatory Project Manager
(301) 594-5333

Sincerely yours

/S/

Robert Temple, M.D
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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APPLICATION NUMBER: NDA 20845

APPROVABLE LETTER

Loui Carter

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 19 99

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We note you submitted manufacturing and controls information, dated February 26, 1997. We also acknowledge receipt of your submissions dated June 10, 17 and 27, July 11 and 31, August 15, 18, 22 (two) and 28 (three), and September 8, 12 (three) and 16 (four), 1997; March 30, April 1 and December 15, 1998; June 1 and 4, August 13, September 27, and November 6, 1999.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The package insert should be identical in content to the enclosed marked-up draft. The immediate container and carton labeling should be identical to the submitted draft (immediate container and carton labels submitted November 6, 1999), except that the storage statement should be changed to the following:

> Store at 25° C (77° F) with excursions permitted between 15-30° C (59-86° F) [see USP Controlled Room Temperature].

This storage statement should be included on all labeling (package insert, and immediate container and carton labels).

The expiration date for drug product stored at 25° C will be 30 months.

Please submit 20 copies of the final printed labeling ten of which are individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not

final print. Please send one copy to the Division of Cardio-Renal Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact:

Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333.

Sincerely yours,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure