

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 29845

CHEMISTRY REVIEW(S)

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-845

DATE REVIEWED: 10-Nov-99

REVIEW #: 4

REVIEWER: JV Advani

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	26-Feb-97	27-Feb-97	03-Mar-97
AMENDMENT (BC)	28-Aug-97	02-Sep-97	04-Sep-97
AMENDMENT (BC)	17-Jun-97	19-Jun-97	24-Jun-97
AMENDMENT (BC)	16-Sep-97	17-Sep-97	18-Sep-97
Resubmission (INO Therapeutics)	25-May-99	26-May-99	04-Jun-99
AMENDMENT (BC)	13-Aug-99	17-Aug-99	20-Aug-99
AMENDMENT (BC)	27-Sep-99	28-Sep-99	30-Sep-99
AMENDMENT (BL)	06-Nov-99	08-Nov-99	10-Nov-99

NAME & ADDRESS OF APPLICANT:

INO Therapeutics, Inc.
54 Old Highway 22
Clinton, NJ 08809
(formerly Ohmeda PPD)

DRUG PRODUCT NAME

Proprietary:

Inhaled Nitric Oxide (INOmax)
This trade name was approved by LNC
Committee on 08/25/97
Nitric oxide
CAS 10102-43-9
I P

Established:

Code Name/#:

Chem.Type/Ther.Class:

PHARMACOL. CATEGORY/INDICATION:

Hypoxemic Respiratory Failure in the Term and near-Term Newborn

DOSAGE FORM:

Inhaled nitric oxide mixtures (nitric oxide in nitrogen)

STRENGTHS:

100 ppm and 800 ppm

ROUTE OF ADMINISTRATION:

Inhaled

Rx/OTC:

Rx OTC

SPECIAL PRODUCTS:

Yes No

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name:

Nitric oxide
Nitrogen (II) oxide

Molecular Formula: NO

Molecular Weight: 30.006

SUPPORTING DOCUMENTS:

Type/Number	Subject	Holder	Status	Review Date	Letter Date
DMF	Seamless, high pressure steel Cylinders (Vol. 1.1 p0104-0106)		*Adequate	-----	
DMF	High pressure, diaphragm seal, stainless steel valve. (Vol. 1.1, p. 0107-01088)		*Adequate	-----	
DMF	O-rings		*Adequate	-----	

* Firm has provided the necessary information in the submission.

RELATED DOCUMENTS (if applicable):

IND (Inhaled Nitric oxide - INO)

IND Inhaled - INO

CONSULTS:

None

REMARKS/COMMENTS:

INOMax is a potent selective pulmonary vasodilator with minimal systemic cardiovascular effects. The drug product is composed of Nitric Oxide (NO) in Nitrogen (N₂) at concentration of either 100 ppm or 800 ppm. It is packaged in aluminum cylinders fitted with a stainless steel valve seated with a Teflon O-ring.

An EER for the establishment of Port Allen, LA, site was requested on 6/15/99 and it is acceptable.

Expiration date: 36 months is proposed. 24 months stability data is provided and 30 months expiration date is acceptable. Methods validation will be requested to be performed by district laboratories.

Amendment of 11/06/99- Firm has submitted on our request the proposed draft labels for cylinders, and for cardboard cylinder box. Also has included the pictures of size 88 cylinders and shrink wrap plastic which will be placed around each cylinder.

CONCLUSIONS & RECOMMENDATIONS:

The information on the draft copies of the labels for drug packages and product is reviewed and is satisfactory. However, we recommend the following storage statement in the labels.

Store at 25°C (77° F) with excursions permitted between 15-30°C (59-86°F) (see USP Controlled Room Temperature). Container labels (gas cylinders) have now been provided and reviewed.

The NDA may be approved from a chemistry viewpoint. The firm should be informed in the action letter that a 30 month expiration date can be granted for the drug product stored at 25° C temperature. And recommended storage statements should be included in the package insert and labels

/S/

JM Advani, Review Chemist

cc:

Orig. NDA 20845

HFD-110/Division File

HFD-110/JADVANI /

HFD-110/PM

HFD-810/TEAM LEADER

HFD-810/DIVISION DIRECTOR (JSimmons)

R/D init by: KSrinivasachar

Filename: NDA20854BC2.Doc

/S/

11-18-99

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NOV - 5 1999

NDA #: 20-845

DATE REVIEWED: 21-Oct-99

REVIEW #: 3

REVIEWER: JV Advani

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CONCLUSIONS & RECOMMENDATIONS:

The information submitted in this resubmission has been previously reviewed (refer to my 2 reviews). The firm has addressed our recommendations that were made during the 1997 submission (refer to review #2 of 10/07/97).

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