DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-024/036

Endo Pharmaceuticals Inc.
100 Painters Drive
Chadds Ford, PA 19317

Attention: Ira C. Lentz
Manager, Regulatory Affairs

Dear Mr. Lentz:

Please refer to your supplemental new drug application dated May 6, 1996, received May 7, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Nubain (nalbuphine hydrochloride) Injection.

We acknowledge receipt of your submissions dated October 24, 1996, and February 25, 2002. Your submission of February 25, 2002, constituted a complete response to our November 26, 2001, action letter.

Reference is also made to the April 14, 2003, telephone conversation between you and Ms. Parinda Jani of this Division.

This supplemental new drug application provides for extensive labeling changes in the **DESCRIPTION, CLINICAL PHARMACOLOGY, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, DRUG ABUSE AND DEPENDENCE, OVERDOSAGE, DOSAGE AND ADMINISTRATION** and **HOW SUPPLIED** sections of the package insert.

We have completed the review of this supplemental application, as amended, and it is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical and include the minor editorial revision indicated, to the draft package insert submitted February 25, 2002. These revisions are terms of the approval of this application.

As agreed, the statement (b)(4)----------
(b)(4)----------will be deleted from the **DESCRIPTION** section.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 18-024/S-036." Approval of this submission by FDA is not required before the labeling is used.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

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

If a letter communicating important information about these drug products (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to appropriate NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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, call Ms. Lisa Basham-Cruz, Regulatory Health Project Manager, at (301) 827-7410.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Acting Director
Division of Anesthetic, Critical Care, and
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bob Rappaport

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