CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-195 & 22-207

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-195
NDA 22-207

NDA APPROVAL

Roxane Laboratories, Inc.
1809 Wilson Rd.
Columbus, OH 43228

Attention: Elizabeth Ernst
Associate Director, DRA-Multisource Products

Dear Ms. Ernst:

Please refer to your new drug applications (NDAs) dated May 16, 2007 (NDA 22-195) and June 7, 2007 (NDA 22-207), received May 17, 2007 (NDA 22-195) and June 8, 2007 (NDA 22-207), submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Morphine Sulfate Oral Solution, 10mg/5 mL and 20 mg/5 mL (NDA 22-195) and Morphine Sulfate Tablets, 15 mg and 30 mg (NDA 22-207).

We acknowledge receipt of your submissions dated May 30, June 8, July 5 and 11, August 21, September 7 and 26, November 2 and 7, and December 11 and 20(2), 2007, and January 7, 28, 29, and 31 and February 7, 8, 14, 22, and 27 (2), 2008, for NDA 22-195, and July 27, August 10 and 30, September 7, November 2, and December 11 and 20 (2), 2007, and January 28 and 31, February 14, 27, and 28 and March 6, 2008, for NDA 22-207.

These new drug applications provide for the use of Morphine Sulfate Oral Solution and Morphine Sulfate Tablets for the relief of moderate to severe acute and chronic pain where an opioid analgesic is appropriate.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions, "SPL for approved NDAs 22-195 and NDA 22-207."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate these submissions "**Final Printed Carton and Container Labels for approved NDAs 22-195 and 22-207.**" Approval of these submissions by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROPRIETARY NAME

If you choose to use a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

PEDIATRIC RESEARCH EQUITY ACT (PREA)

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. We are deferring submission of your pediatric studies for ages 0 to 17 years until March 21, 2013.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

Deferred pediatric study under PREA for the treatment moderate to severe acute and chronic pain where an opioid analgesic is appropriate

1. in pediatric patients ages 0 to 17.

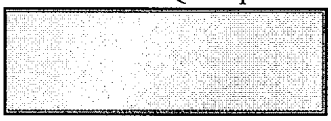
   Final Report Submission: March 31, 2013.

Submit final study reports to these NDAs. For administrative purposes, all submissions related to these pediatric postmarketing study commitments must be clearly designated "**Required Pediatric Study Commitments**".

POSTMARKETING COMMITMENTS

We remind you of your postmarketing study commitment in your email dated March 17, 2008. This commitment is listed below.

2. Description of Commitment: a minimal genetic toxicology screen (two in vitro genetic toxicology studies, e.g., one point mutation assay and one chromosome aberration assay) tested up to the limit dose for the assay, for each of the following drug substance impurities that exceed ICHQ3A qualification thresholds of NMT 0.15%:



b(4)

Study Start: by June 30, 2008
Final Report Submission: by December 31, 2008

Submit clinical and nonclinical protocols to your IND for these products. Submit chemistry, manufacturing, and controls protocols and all study final reports to the pertinent NDAs. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

An expiration dating period of 36 months is granted to the Morphine Sulfate Oral Solution (NDA 22-195) when the product is stored at room temperature, 20- 25°C (68- 77°F) in the approved container closure systems described in the NDA. With accrual of additional real time stability data, you may extend the expiration dating period and report it in an annual report.

An expiration dating period of 18 months is granted to the Morphine Sulfate Tablets (NDA 22-207) when the product is stored at room temperature, 20- 25°C (68- 77°F) in the approved container closure systems described in the NDA. With accrual of additional real time stability data, you may extend the expiration dating period and report it in an annual report.

In addition, we remind you of your agreement to amend both NDAs to include, in the first annual report, an updated validation technical report which will contain data to demonstrate the accuracy, linearity, precision, and a limit of quantitation for morphinone.

If you issue a letter communicating important safety related information about these drug products (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to the pertinent NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

Sharon Hertz
3/17/2008 05:20:13 PM
Signing for Bob Rappaport, M.D.