Boehringer Ingelheim
Roxane Laboratories

Sharon Hertz, M.D.
Director
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Building 22, Room 3119
Silver Springs, MD 20933-0002

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Jerald Andry, PharmD, MS
Executive Director, Drug Regulatory Affairs and Medical Affairs

Telephone 614-241-4154
Fax 614-276-2470
E-Mail jerry.andry@boehringer-ingelheim.com

1809 Wilson Road
Columbus, Ohio 43228

RESPONSE TO PREA NON-COMPLIANCE LETTER

RE: NDA 022195/S-010: Morphine Sulfate Oral Solution, 10 mg/5mL, 20 mg/5 mL, and 100 mg/5 mL
NDA 022207/S-005: Morphine Sulfate Tablets, 15 mg and 30 mg

Dear Dr. Hertz:

Reference is made to NDA 22-195 for Morphine Sulfate Oral Solution and NDA 22-207 for Morphine Sulfate Oral Tablets approved on March 17, 2008 and the deferred pediatric studies under the Pediatric Research Equity Act (PREA) for pediatric patients ages 2 to 17 years and from birth to 2 years.

The purpose of this letter is to respond to the Agency's **Notification of Non-Compliance** with PREA letter, dated February 5, 2016.

Roxane Laboratories' submission of pediatric study reports on August 28, 2012 provided safety and pharmacokinetic data in pediatric patients ages 2 through 17 years. As noted in the **FDA's letter** of January 21, 2016, the agency found the information provided in this study as insufficient to meet the PREA requirements because the [redacted] (b) (4) Therefore, Roxane Laboratories must repeat a multiple-dose safety and pharmacokinetic study [redacted] (b) (4)

Roxane Laboratories is requesting a deferral extension as the study in the target patient population of pediatric patients ages 2 to 17 years needs to be repeated. Roxane Laboratories expects to submit the required pediatric assessment by the following dates:

1. Deferred pediatric study of pharmacokinetics and safety under PREA for the treatment of moderate to severe pain where an opioid analgesic is appropriate in pediatric patients ages 2 to 17 years

   Final Protocol Submission Date: June 2016
   Study Initiation Date: April 2017
   Final Report Submission Date: July 2018

2. Deferred pediatric study of pharmacokinetics, safety and efficacy under PREA for the treatment of moderate to severe pain where an opioid analgesic is appropriate in pediatric patients ages birth to 2 years

   2a. Deferred pediatric study of pharmacokinetics and safety under PREA for the treatment of moderate to severe pain where an opioid analgesic is appropriate in pediatric patients ages birth to 2 years

   Final Protocol Submission Date: September 2018
   Study Initiation Date: July 2019
   Final Report Submission Date: December 2020

   2b. Deferred pediatric study of efficacy and safety under PREA for the treatment of moderate to severe pain where an opioid analgesic is appropriate in pediatric patients ages birth to 2 years

   Final Protocol Submission Date: February 2021
   Study Initiation Date: December 2021
   Final Report Submission Date: May 2023

Roxane Laboratories remains committed to fulfilling its post-marking obligations under PREA. Correspondence concerning this response should be directed to Jerald Andry, Executive Director, Drug Regulatory Affairs and Medical Affairs at (614) 241-4154, by fax at (614) 276-2470, or by email at Jerry.Andry@boehringer-ingelheim.com.

Respectfully,

Jerald Andry, PharmD, MS
Executive Director, Drug Regulatory Affairs and Medical Affairs
Roxane Laboratories, Inc.