DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 50-585/S-059

Hoffmann-La Roche, Inc.
Attention: Lynn DeVenezia-Tobias
Program Manager, Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. DeVenezia-Tobias:

Please refer to your supplemental new drug application dated January 18, 2007, received January 19, 2007 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Rocephin® (ceftriaxone sodium) vials, 250 mg, 500 mg, 1g and 2g.

This application is subject to the exemption provisions contained in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We also acknowledge receipt of your submissions dated April 24, 2007 and May 1, 2007, containing a translated version of the current Swiss prescribing information for Rocephin®, information regarding physical incompatibility with infusion solutions containing Ca^{++}-ions, and a copy of your proposed "Dear Health Care Professional" letter.

This supplemental new drug application provides for the following:

- Addition of new information in the CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION sections of the label to describe the potential risk associated with concomitant use of Rocephin® with calcium or calcium containing products.

- Addition of new text to the CONTRAINDICATIONS section, in the "Pediatric Use" subsection in particular to more prominently reinforce that hyperbilirubinemic neonates, especially prematures, should not be treated with Rocephin®.

We completed our review of this application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text, and with the following editorial revisions (see corresponding line numbers for exact revision locations). Deletion is indicated by strikethrough and addition is underlined:

1. CONTRAINDICATIONS (lines 294 and 295): Rocephin should not be administered concurrently with ~~calcium treatment~~ calcium-containing solutions or products in newborns because of the risk of precipitation of ceftriaxone-calcium salt (see WARNINGS).

2. WARNINGS (lines 319 to 325 should be moved and presented in bold font as new paragraphs following line 304 as follows):

   Ceftriaxone must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines.

   Calcium-containing solutions or products must not be administered within 48 hours of last administration of ceftriaxone.

   Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidneys in [redacted] both term and premature neonates have been described.

3. ADVERSE REACTIONS (lines 434 and 435): Cases of fatal reactions with calcium-ceftriaxone precipitates in lung and kidneys in ~~neonates and prematures~~ both term and premature neonates have been described.

4. DIRECTIONS FOR USE AND COMPATIBILITY AND STABILITY (following line 474 and line 522, respectively): **Do not use diluents containing calcium, such as Ringer's solution or Hartmann's solution, to reconstitute Rocephin. Particulate formation ~~will~~ can result.**

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the enclosed labeling submitted on January 18, 2007. These revisions are terms of the approval of this application.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. For administrative purposes, designate this submission "**FPL for approved supplement NDA 50-585/S-059.**" Approval of this submission by FDA is not required before the labeling is used.

As previously stated, we acknowledge receipt of your "Dear Health Care Professional" letter via electronic mail on May 1, 2007. We recommend that this letter be revised to be consistent with the approved changes to the package insert described above. We request that you submit a revised copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
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 J. Christopher Davi, MS, Regulatory Project Manager, at (301) 796-0702.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Proposed package insert submitted January 18, 2007

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

/s/

Janice Soreth
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