DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-591/S-027

Hoffmann-La Roche Inc.
Attention: Ms. Lynn DeVenezia-Tobias
Senior Program Manager, Diversified Products
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Ms. DeVenezia-Tobias:

Please refer to your supplemental new drug application (sNDA) dated April 23, 2009, received April 24, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lariam® (mefloquine hydrochloride) Tablets, 250 mg.

This supplemental new drug application (sNDA) provides for revisions to the Lariam® labeling to update the **DOSAGE AND ADMINSTRATION**/Pediatric Patients and **DOSAGE AND ADMINISTRATION**/Pediatric Patients/Malaria Prophylaxis subsections to include information that reflects text supported by current data.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. This application provides for the following revisions to the content of labeling for the package insert (additions are noted with underline and deletions are noted with ~~strikethrough~~):

1. Under the **DOSAGE AND ADMINISTRATION**/Pediatric Patients subsection:

   Pediatric Patients

   Treatment of mild to moderate malaria in pediatric patients caused by mefloquine-susceptible strains of *P. falciparum.*

   Twenty (20) to 25 mg/kg body weight. Splitting the total therapeutic dose into 2 doses taken 6 to 8 hours apart may reduce the occurrence or severity of adverse effects. Experience with Lariam in pediatric patients ~~infants less than 3 months old or~~ weighing less than 20~~5~~ kg is limited. The drug should not be taken on an empty stomach and should be administered with ample water. The tablets may be crushed and suspended in a small amount of water, milk or other beverage for administration to small children and other persons unable to swallow them whole.

2. Under the **DOSAGE AND ADMINISTRATION**/Pediatric Patients/Malaria Prophylaxis subsection:

   Malaria Prophylaxis

   ~~The following doses have been extrapolated from the recommended adult dose. Neither the pharmacokinetics, nor the clinical efficacy of these doses has been determined in children owing to the difficulty of acquiring this information in pediatric subjects.~~ The recommended prophylactic dose of Lariam is approximately 5 mg/kg body weight once weekly. One 250 mg Lariam tablet should be taken once weekly in pediatric patients weighing over 45 kg. In pediatric patients weighing less than 45 kg, the weekly dose decreases in proportion to body weight:

   30 to 45 kg: 3/4 tablet
   20 to 30 kg: 1/2 tablet
   ~~10 to 20 kg: 1/4 tablet~~
   ~~5 to 10 kg: 1/8 tablet~~[*]

   [*] ~~Approximate tablet fraction based on a dosage of 5 mg/kg body weight. Exact doses for children weighing less than 10 kg may best be prepared and dispensed by pharmacists.~~

   Experience with Lariam in pediatric patients ~~infants less than 3 months old or~~ weighing less than 20 ~~5~~ kg is limited.

   Revised: Month/Year ~~September 2008~~

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit 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 in content 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 this submission "**SPL for approved supplement NDA 19-591/S-027**."

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in SPL format to include the changes approved in this application. Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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

(b) (4) Please submit an amendment to that supplement to update the text of the labeling to include the revisions approved in this supplement.

If you have any questions, call Mr. Gregory DiBernardo, Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure