CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-799

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-799

Mutual Pharmaceutical Company, Inc.
Attention: Mr. Robert Dettery
Vice President, Regulatory Affairs
1100 Orthodox Street
Philadelphia, PA 19124

Dear Mr. Dettery:

Please refer to your new drug application (NDA) dated October 13, 2004 received October 14, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Quinine Sulfate Capsules, 324 mg.

We acknowledge receipt of your submissions dated:

November 24, 2004	April 29, 2005	June 22, 2005
January 27, 2005	May 27, 2005	July 6, 2005
March 28, 2005	June 7, 2005	July 21, 2005
March 30, 2005	June 17, 2005	August 11, 2005

This new drug application provides for the use of Quinine Sulfate for treatment of uncomplicated *Plasmodium falciparum* malaria.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-799.**" Approval of this submission by FDA is not required before the labeling is used.

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.

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 or has been granted orphan drug status. As this application has been granted orphan drug status, you do not have to comply with this requirement.

We remind you of your postmarketing study commitments in your submission dated August 11, 2005. These commitments are listed below.

1. Develop a **Risk Management Plan** that includes the following elements:

   - An educational program directed at physicians and other health care providers regarding the safe and effective use of quinine sulfate for treatment of *Plasmodium falciparum* malaria.

   - A written "Dear Doctor" Letter to physicians describing the favorable risk/benefit ratio of oral quinine sulfate for treatment of *P. falciparum* malaria; in contrast with the unfavorable risk/benefit ratio for treatment of nocturnal leg cramps.

     Implementation date: August 11, 2006

2. Conduct **Post-marketing Surveillance** for Adverse Events:

   Provide twice-yearly analyses for three years post-approval of post-marketing adverse event data, including assessment of possible causal relationship of adverse events to quinine sulfate, analysis of adverse events by age (< 16, 16 to 65 and > 65 years old) and by indication for quinine use. These analyses are requested in conjunction with the quarterly updates of post-marketing adverse events associated with oral quinine sulfate required under 21 CFR 314.80(c)(2) and in addition to the 15-day reporting for all serious adverse events required under 21 CFR 314.80(c)(1).

   Initial study report submission date: February 2006
   Final report submission date: February 2009

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 must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Promotional materials must be consistent with the final product labeling and patient package insert, particularly with regard to the approved indications, as well as the safety issues associated with quinine sulfate use. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

The Division acknowledges Mutual's intent to cease distribution of and to cancel all outstanding orders for all unapproved quinine sulfate products manufactured by Mutual. The Division notes that this approach is consistent with maintaining the integrity of the drug approval process.

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, please call Kristen Miller, Pharm.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

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

Enclosure:
Package Insert
Patient Package Insert

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

/s/

Renata Albrecht
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NDA 21-799