DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021799/S-011

AR Holding Company, Inc.
c/o 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 Supplemental New Drug Application (sNDA) dated June 8, 2009, received June 9, 2009 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Qualaquin® (quinine sulfate USP) Capsule, 324 mg.

We also acknowledge receipt of your submissions dated:

July 10. 2009	March 19, 2010 (2)
August 18, 2009	April 29, 2010
December 18, 2009	May 19, 2010
February 22, 2010	June 2, 2010

The December 18, 2009 submission constituted a complete response to our September 23, 2009 action letter.

This supplemental new drug application provides for the following revisions to the Qualaquin® (quinine sulfate USP) Medication Guide: (additions are noted by underline and deletions are noted by ~~strikethrough~~)

1. Under **QUALAQUIN® used to treat or prevent leg cramps may cause serious side effects or even death.**

    - QUALAQUIN® may cause your blood cell (platelet) count to drop causing serious bleeding problems. ~~In some cases, kidney injury can occur.~~ In some people, serious kidney problems can happen.

2. Under **Tell your healthcare provider about all the medicines you take, including prescription medicines, vitamins and herbal supplements.** ~~See "What is the most important information I should know about QUALAQUIN®?"~~

3. Under **QUALAQUIN® may cause serious side effects.**

    - See "What is the most important information I should know about QUALAQUIN®" section.
    - Low blood sugar (hypoglycemia). This can include sweating, weakness, nausea, vomiting, or confusion (b) (4) .

4. Editorial Revisions are included in the attached Medication Guide.

We have completed our review of this supplemental application, as amended. It is 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, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). The details of the REMS requirements were outlined in our REMS notification letter dated September 23, 2009.

Since Qualaquin® (quinine sulfate USP) was approved on August 12, 2005, we have become aware, through a review of Adverse Event Reporting System (AERS) data, of adverse events of serious and life-threatening hematologic reactions, including thrombocytopenia and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP) associated with the use of Qualaquin® (quinine sulfate USP). Chronic renal impairment associated with the development of TTP has been reported. We consider this information to be "new safety information" as defined in section 505-1(b) of FDCA.

Your proposed REMS, submitted on December 18, 2009 and amended on February 22, 2010, March 19, 2010 (2), April 29, 2010, May 19, 2010, and June 2, 2010 and appended to this letter, is approved. The REMS consists of a Medication Guide, a communication plan, and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include but is not limited to the following:

a. An evaluation of patients' and healthcare providers' understanding of the serious risks of Qualaquin® (quinine sulfate USP)
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance
d. An evaluation of serious adverse events reported with the use of Qualaquin® (quinine sulfate USP)
e. An evaluation of the prescription data to evaluate the numbers of prescriptions dispensed, diagnoses associated with Qualaquin® (quinine sulfate USP) prescriptions, and prescriber's specialty.
f. Verification of sources of recipient lists
g. Number of recipients on each mailing list
h. Date(s) of mailing(s)
i. Copy of document(s) included in the mailing(s)

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

NDA 021799 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021799
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE) FOR NDA 021799
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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 http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
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).

If you have any questions, call Hyun Son Pharm.D., Safety Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, M.D., MPH
Deputy Director for Safety
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURES:
Package Insert
REMS Document

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21799	SUPPL-11	AR HOLDING CO INC	QUALAQUIN SULFATE CAPSULES 324MG

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

/s/

OZLEM A BELEN
06/15/2010