DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-078/S-016

GlaxoSmithKline
Attention: Debra Hackett
Director, U.S. Regulatory Affairs
One Franklin Plaza, 200 N. 16th Street
Philadelphia, PA 19102

Dear Ms. Hackett:

Please refer to your supplemental new drug application dated and received June 30, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Malarone® (atovaquone and proguanil hydrochloride) Tablets.

This "Changes Being Effected" supplemental new drug application provides for the following changes to the package insert (additions are noted by underline and deletions are noted by ~~strikethrough~~):

1. In the **ADVERSE REACTIONS/Post-Marketing Adverse Reactions:** ***Immune System Disorders*** subsection the paragraph is modified as follows:

   Allergic reactions including angioedema, urticaria, and rare cases of anaphylaxis and vasculitis.

2. In the **ADVERSE REACTIONS/Post-Marketing Adverse Reactions** subsection, an additional subsection was added as follows:

   Gastrointestinal Disorders: Stomatitis.

3. In the **ADVERSE REACTIONS/Post-Marketing Adverse Reactions/*Hepatobiliary Disorders*** subsection the paragraph is modified as follows:

   Elevated liver function tests and rare cases of hepatitis, cholestasis; a single case of hepatic failure requiring transplant has been reported.

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 submitted on June 30, 2008.

Within 21 days of 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. Upon receipt and verification, we will transmit that

version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions "**SPL for approved supplement NDA 21-078/S-016**."

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

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 Sherry Spriggs, Regulatory Project Manager, at (301) 796-4018.

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: 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

12/18/2008 11:43:47 AM