DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21-078/S-017 **SUPPLEMENT APPROVAL**

SmithKline Beecham Corporation
d/b/a GlaxoSmithKline
Attention: Ms. Debra S. 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 on March 5, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Malarone® (atovaquone and proguanil hydrochloride) Tablets.

We acknowledge receipt of your submission dated August 31, 2009.

This application provides for the following revisions to the package insert of Malarone (additions are noted with underline and deletions are noted with ~~strikethrough~~).

1. In the **PRECAUTIONS/Carcinogenesis, Mutagenesis, Impairment of Fertility/ Proguanil** subsection, a fourth paragraph is added as follows:

   A fertility study in Sprague-Dawley rats revealed no adverse effects at doses up to 16 mg/kg/day of proguanil hydrochloride (up to 0.2-times the average human exposure based on AUC comparisons). Fertility studies of proguanil in animals at exposures similar to or greater than those observed in humans have not been conducted.

2. In the **PRECAUTIONS/Pregnancy** subsection, a third paragraph is added as follows:

   A pre- and post-natal study in Sprague-Dawley rats revealed no adverse effects at doses up to 16 mg/kg/day of proguanil hydrochloride (up to 0.2-times the average human exposure based on AUC comparisons). Pre- and post-natal studies of proguanil in animals at exposures similar to or greater than those observed in humans have not been conducted.

We have 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 enclosed labeling text, which is identical to the content of labeling in structured product labeling (SPL) format submitted on August 31, 2009, under 21 CFR 314.50(l)(1)(i).

To facilitate the transmission of labeling to the National Library of Medicine for public dissemination, please resubmit the enclosed content of labeling in SPL format as soon as possible, but no later than 14 days from the date of this letter. For administrative purposes, please designate this submission, "**SPL for approved NDA 21-078/S-017.**"

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 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: 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
09/02/2009