DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-651/S-016

Procter & Gamble Pharmaceuticals, Inc.
Attention: Victoria Ireland
Manager, Regulatory Affairs
8700 Mason-Montgomery Road
Mason, Oh 45040-9462

Dear Ms. Ireland:

Please refer to your supplemental new drug application dated October 6, 2006, received October 10, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Asacol (mesalamine) Delayed Release Tablets, 400 mg.

We acknowledge receipt of your submission dated December 18, 2006.

This "Changes Being Effected" supplemental new drug application provides for revisions to the package insert with the addition of safety information to align the US label with the UK label.

We completed our review of this supplemental new drug application, as amended. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on December 18, 2006. However, please note that during the review of the package insert, we found the wording used in Carcinogenesis, mutagenesis, impairment of fertility subsection and Pregnancy: Teratogenic Effects: Pregnancy Category B subsection under the PRECAUTIONS section is not in line with the recommended wording in the regulations under 21 CFR Subpart 201.57 nor the currently used CDER wording for the preclinical portions of the labeling. We therefore ask that the text in these subsections be revised as follows:

> Carcinogenesis, mutagenesis, impairment of fertility: Dietary mesalamine was not carcinogenic in rats at doses as high as 480 mg/kg/day, or mice at 2000 mg/kg/day. These doses are 2.4 and 5.1 times the maximum recommended human maintenance dose of Asacol of 1.6 g/day (32 mg/kg/day if 50 kg body weight assumed or 1184 mg/m^2), respectively, based on body surface area.
>
> Mesalamine was negative in the Ames assay for mutagenesis, negative for induction of sister chromatid exchanges (SCE) and chromosomal aberrations in Chinese hamster ovary (CHO) cells *in vitro*, and negative for induction of micronuclei (MN) in mouse bone marrow polychromatic erythrocytes.
>
> Mesalamine, at oral doses up to 480 mg/kg/day (about 1.6 times the recommended human treatment dose on a body surface area basis), ~~had no adverse~~ was found to have no effect on fertility or reproductive performance of male or female rats.

> Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproduction studies have been performed in rats at oral doses up to 480 mg/kg/day (about 1.6 times the recommended human treatment dose on a body surface area basis) and rabbits at oral doses up to 480 mg/kg/day (about 3.2 times the recommended human treatment dose on a body surface area basis) and have revealed no evidence of ~~teratogenic effects~~ impaired fertility or ~~fetal toxicity~~ harm to the fetus due to mesalamine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Please revise the above text with the next printing of the package insert and notify the Agency when it has been completed.

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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Kristen Everett, Regulatory Project Manager, at (301) 796-0453.

Sincerely,

{See appended electronic signature page}

Brian E. Harvey, M.D., Ph.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

Brian Harvey
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