DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-742/S-019
NDA 50-742/S-021

Merck & Co., Inc.
Attention: Peter Kusma
Manager, Regulatory Affairs
PO Box 1000, UG2CD-48
North Wales, PA 19454-1099

Dear Mr. Kusma:

Please refer to your supplemental new drug applications dated and received on March 27, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for STROMECTOL™ (ivermectin) 3 mg and 6 mg Tablets. We acknowledge receipt of your submissions dated September 14, 2007.

We note that although this supplemental application was submitted as a changes being effected (CBE) supplemental NDA, changes that reflect the discontinuation of the 6 mg tablets were reviewed under a prior approval supplemental NDA (21 CFR 314.70). Therefore, we administratively split the original application as follows:

A. NDA 50-742/S-019 - Changes Being Effected Supplement

This "Changes Being Effected" supplemental new drug application provides for the following change: (double underlined = added text, ~~strikethrough~~ = deleted text):

1. In the **PRECAUTIONS**/*General* subsection, the second paragraph has been revised as follows:

   Rarely, patients with onchocerciasis who are also heavily infected with Loa loa may develop a serious or even fatal encephalopathy either spontaneously or following treatment with an effective microfilaricide. In these patients, the following adverse experiences have also been reported: ~~back~~ pain (including neck and back pain), red eye, conjunctival hemorrhage, dyspnea, urinary and/or fecal incontinence, difficulty in standing/walking, mental status changes, confusion, lethargy, stupor, seizures, or coma. This syndrome has been seen very rarely following the use of ivermectin. In individuals who warrant treatment with ivermectin for any reason and have had significant exposure to Loa loa-endemic areas of West or Central Africa, pretreatment assessment for loiasis and careful post-treatment follow-up should be implemented.

B. NDA 50-742/S-021 - Prior Approval Supplement

This "Prior Approval" supplemental new drug application provides for the following changes: (double underlined = added text, ~~strikethrough~~ = deleted text):

1. In the **DESCRIPTION** section, the third paragraph has been revised as follows:

   STROMECTOL is available in 3-mg tablets ~~and 6-mg scored tablets. Each tablet contains~~ containing the following inactive ingredients: microcrystalline cellulose, pregelatinized starch, magnesium stearate, butylated hydroxyanisole, and citric acid powder (anhydrous).

2. In the **CLINICAL PHARMACOLOGY**/*Pharmacokinetics* subsection, the first paragraph has been revised as follows:

   Following oral administration of ivermectin, plasma concentrations are approximately proportional to the dose. In two studies, after 12-mg doses of STROMECTOL ~~(2x6mg)~~ in fasting healthy volunteers (representing a mean dose of 165 mcg/kg), the mean peak plasma concentration of the major component (H_2B_{1a}) were 46.6 (±21.9) (range: 16.4-101.1) and 30.6 (±15.6) (range: 13.9-68.4) ng/mL, respectively, at approximately 4 hours after dosing.

3. In the **DOSAGE AND ADMINISTRATION** section, Table 1 and Table 2 have been revised as follows:

Table 1
Dosage Guideline for STROMECTOL for Strongyloidiasis

Body Weight (kg)	Single Oral Dose Number of 3-mg Tablets	~~Number of 6-mg Tablets~~
15-24	1 Tablet	~~½ Tablet~~
25-35	2 Tablets	~~1 Tablet~~
36-50	3 Tablets	~~1½ Tablets~~
51-65	4 Tablets	~~2 Tablets~~
66-79	5 Tablets	~~2½ Tablets~~
≥ 80	200 mcg/kg	~~200 mcg/kg~~

Table 2
Dosage Guideline for STROMECTOL for Onchocerciasis

Body Weight (kg)	Single Oral Dose Number of 3-mg Tablets	~~Number of 6-mg Tablets~~
15-25	1 Tablet	~~½ Tablet~~
26-44	2 Tablets	~~1 Tablet~~
45-64	3 Tablets	~~1½ Tablets~~
65-84	4 Tablets	~~2 Tablets~~
≥ 85	150 mcg/kg	~~150 mcg/kg~~

4. In the **HOW SUPPLIED** section, reference to the 6 mg has been deleted as follows:

~~No. 8107 — Tablets STROMECTOL 6 mg are white, scored, round, flat, bevel edged tablets coded MSD 139 on one side and scored on the other. They are supplied as follows:~~
~~NDC 0006-0139-10 unit dose package of 10.~~

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Hyun Son, Pharm.D., 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
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