DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 11-145/S-090 & 091
NDA 11-870/S-036

Merck & Co., Inc.
Attention: Mr. Kenneth A. Kramer
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Mr. Kramer:

Please refer to your electronic supplemental new drug applications dated August 12, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

Diuril (chlorothiazide) 250 & 500 mg Tablets (NDA 11-145/S-090)
Diuril (chlorothiazide) 0.5 g/vial Intravenous Injection (NDA 11-145/S-091)
Diuril (chlorothiazide) 250 mg/5mL Oral Suspension (NDA 11-870/S-036)

We acknowledge receipt of your submissions dated January 12 and April 29, 2004 (NDA 11-145/S-090 & 11-870/S-036), and January 12, and May 14, 2004 (NDA 11-145/S-091). Your submissions of April 29, 2004 (NDA 11-145/S-090 & 11-870/S-036), and May 14, 2004 (NDA 11-145/S-091) constituted a complete response to our December 30, 2003 action letter.

These electronic supplemental new drug applications provide for final printed labeling (FPL) revised to add a *Geriatric Use* sub-section at the end of the **PRECAUTIONS,** as follows:

NDA 11-145/S-090 (Tablets)
NDA 11-870/S-036 (Oral Suspension)

Clinical studies of DIURIL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see WARNINGS).

NDA 11-145/ S-091 (Intravenous)

> Clinical studies of Intravenous Sodium DIURIL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.
>
> This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see WARNINGS).

We have completed our review of these electronic supplemental new drug applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on April 29, 2004 (NDA 11-145/S-090 & 11-870/S-036), and May 14, 2004 (NDA 11-145/S-091).

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, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

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, please call:

Mr. Daryl Allis
Regulatory Project Manager
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
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/

Norman Stockbridge

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