DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-200/S-024
NDA 18-201/S-037

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 supplemental new drug applications dated June 28, 2001 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Midamor (amiloride hydrochloride) 5 mg Tablets and Moduretic (amiloride hydrochloride and hydrochlorothiazide) 5/50 mg Tablets.

We acknowledge receipt of your submission dated February 5, 2002 that constituted a complete response to our August 7, 2001 action letter.

These supplemental new drug applications provide for final printed labeling revised as follows:

NDA 18-200/S-024 (Midamor)

Added **PRECAUTIONS**/Geriatric Use sub-section:

Geriatric Use

Clinical studies of Midamor did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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 CONTRAINDICATIONS, Impaired Renal Function.)

NDA 18-201/S-037 (Moduretic)

Added **PRECAUTIONS**/Geriatric Use sub-section:

Geriatric Use

Clinical studies of Moduretic did not include sufficient numbers of subjects aged 65 and over to determine whether they responded 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 CONTRAINDICATIONS, Impaired Renal Function.)

We also noted minor editorial changes.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling included in your February 5, 2002 submission. Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
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 Health Project Manager
(301) 594-5309

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton, M.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/

Doug Throckmorton

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