DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 11-145/S-092

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 application dated June 3, 2004, received June 4, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diruil™ (chlorothiazide) 0.5 g/vial intravenous Injection and 250 and 500 mg tablets.

This supplemental new drug application submitted as "Changes Being Effected" provides for electronic final printed labeling revised to clarify the need for the immediate use after reconstitution of the preservative-free solution under the **DOSAGE AND ADMINISTRATION** and **HOW SUPPLIED** sections of the package insert and the carton and container labeling for the intravenous injection (only) as follows:

Package Insert

1. Under the **DOSAGE AND ADMINISTRATION** section:
    - Added a new subheading, "*Directions for Reconstitution*" and a highlighted statement regarding the need for aseptic technique and the immediate use of the reconstituted solution as follows:

        Directions for Reconstitution
        Use aseptic technique. Because Intravenous Sodium DIURIL contains no preservative, a fresh solution should be prepared immediately prior to each administration, and the unused portion should be discarded.

    - The following text, was moved to immediately precede the "*Directions for Reconstitution*":

        Extravasation must be rigidly avoided. Do not give subcutaneously or intramuscularly.

        The usual adult dosage is 0.5 to 1.0 g once or twice a day. Many patients with edema respond to intermittent therapy, i.e., administration on alternate days or on three to five days each week. With an intermittent schedule, excessive

response and the resulting undesirable electrolyte imbalance are less likely to occur.

2. Under the **HOW SUPPLIED**, Storage section, the statement, "Use solution immediately after reconstitution. (See DOSAGE AND ADMINISTRATION, Directions for Reconstitution.)", was added.

3. The following minor editorial changes are noted:

    - The Manufacturer address was changed from "West Point, PA 19486, USA" to "Whitehouse Station, NJ 08889, USA."
    - Under the DESCRIPTION section, the empirical formula was corrected by removing the duplicate "N_3."
    - Under the PRECAUTIONS/ General section, 3rd paragraph, a hyphen was added to "potassium-sparing."
    - The Issued date was updated to April 2004.

Carton and Container Labels

1. The text "Discard unused portion of the reconstituted solution" was replaced with "Use reconstituted solution ***immediately***. Discard unused portion."

2. The Manufacturer address was changed from "West Point, PA 19486, USA" to Whitehouse Station, NJ 08889, USA.

We completed our review of this supplemental new drug application, as amended and it is approved, effective on the date of this letter, for use as recommended in the electronic final printed labeling (FPL) submitted on June 3, 2004.

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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