DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-238/S-031

KV Pharmaceutical Company
Attention: Mr. Angel L. Rodriguez
2503 South Hanley Road
St. Louis, MO 63144-2555

Dear Mr. Rodriguez:

Please refer to your supplemental new drug application dated May 9, 2003 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Micro-K Extencaps (potassium chloride, USP) 600 mg (8 mEq) Extended-Release Capsules and Micro-K 10 Extencaps (potassium chloride, USP) 750 mg (10 mEq) Extended-Release Capsules.

We also refer to your submission dated June 13, 2003.

This "Changes Being Effected" supplemental new drug application provides for final printed labeling revised by adding the following paragraph to the end of the OVERDOSAGE section as requested in our Supplement Request Letter dated February 11, 2003:

> The extended release feature means that absorption and toxic effects may be delayed for hours. Consider standard measures to remove any unabsorbed drug.

In addition the following changes are noted:

1. The text "U.S. Patent 4,259,315" was moved from the end of the package and inserted under the established name at the beginning of the package insert.

2. The text "Caution: Federal law prohibits dispensing without prescription" was deleted at the end of the package insert, and the text "Rx Only" was added to the beginning of the package insert.

3. Under the **PRECAUTIONS/ Information For Patients** section, the single information statements were combined into one paragraph to read:

   > Physicians should consider reminding the patient of the following: To take each dose with meals and with a full glass of water or other suitable liquid. To take each dose without crushing, chewing, or sucking the capsules. To take this medicine following the frequency and amount prescribed by the physician. This is especially important if the patient is also taking diuretics and/or digitalis preparations. To check with the physician if there is trouble swallowing capsules or if the capsules seem to stick in the throat.

4. Under the **PRECAUTIONS/ Laboratory Tests** section, the sentences were combined into one paragraph to read:

   > Regular serum potassium determinations are recommended, especially in patients with renal insufficiency or diabetic nephropathy. When blood is drawn for analysis of plasma potassium it is

important to recognize that artifactual elevations can occur after improper venipuncture technique or as a result of in vitro hemolysis of the sample.

5. Under the **ADVERSE REACTIONS** section, the "most common adverse reactions" and "reported rarely" events were combined into one paragraph to read:

   The most common adverse reactions to the oral potassium salts are nausea, vomiting, flatulence, abdominal discomfort, and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by taking the dose with meals, or reducing the amount taken at one time. Skin rash has been reported rarely with potassium preparations.

6. Under the **OVERDOSAGE** section, the second and third paragraphs were combined into one paragraph to read:

   Treatment measures for hyperkalemia include the following: (1) elimination of foods and medications containing potassium and of any agents with potassium sparing properties; (2) intravenous administration of 300 to 500 mL of 10% dextrose solution containing 10 to 20 units of crystalline insulin per 1,000 mL; (3) correction of acidosis, if present, with intravenous sodium bicarbonate; (4) use of exchange resins, hemodialysis, or peritoneal dialysis. In treating hyperkalemia, it should be recalled that in patients who have been stabilized on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

7. Under the **DOSAGE AND ADMINISTRATION** section, the second and third paragraphs were combined into one paragraph to read:

   Dosage must be adjusted to the individual needs of each patients. The dose for the prevention of hypokalemia is typically in the range of 20 mEq per day. Doses of 40 to 100 mEq per day or more are used for the treatment of potassium depletion. Dosage should be divided if more than 20 mEq is given in a single dose. Because of the potential for gastric irritation (see WARNINGS), Micro-K Extencaps should be taken with meals and with a full glass of water or other liquid.

8. Under the **HOW SUPPLIED** section:
   - The capsule monograms were changed from "AHR/5720" and "AHR/5730" to "Ther-Rx"/ "010" and "Ther-Rx"/ "009" for the 600 mg (8 mEq) and 750 mg (10 mEq) capsules, respectively.

   - The manufacturer information was changed from:

     Pharmaceutical Division
     A.H. Robins Company
     Richmond, VA 23220

     To:

     Manufactured by KV Pharmaceutical
     For THER-RX Corporation
     St. Louis, MO 63045

   - The NDC numbers, manufacturer code and revised date were updated according to the change in the manufacturer

In addition, we note that under the **PRECAUTIONS** section, the following subsection was added:

> **Geriatric Use** Clinical studies of Potassium Chloride Extended-release Capsules 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.

We have 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 final printed labeling (FPL) submitted on May 9, 2003.

We also request, at the next time of printing, that you revise the labeling as follows:

1. Under the **Geriatric Use** section, replace "Potassium Chloride Extended-release Capsules" with "Micro-K Extencaps.

2. Delete the "s" in the word "patients" in the second paragraph under the **DOSAGE AND ADMINISTRATION** section.

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, 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
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation 1
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

8/20/03 12:37:45 PM