DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-678/S-014
NDA 20-734/S-013

Baxter Healthcare Corporation
Route 120 & Wilson Road; RLT-10
Round Lake, IL 60073

Attention: Marcia Marconi
Vice President, Regulatory Affairs

Dear Ms. Marconi:

Please refer to your supplemental new drug applications dated July 22, 2003, received July 23, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clinimix - sulfite free and Clinimix E – sulfite free Injections.

Reference is also made to the January 22, 2004, telephone conversation between Ms. Parinda Jani of this Division and Ms. Mary Konkowski of your company.

These supplemental new drug applications provide for the following revisions to the package insert.

1. In the **CONTRAINDICATIONS** section, a statement regarding corn allergies is added.

2. In the **PRECAUTIONS** section, the statement regarding fluid and/or solute overloading is revised and a **"Geriatric Use"** subsection is added in accordance with the requirements of 21 CFR 201.57(f)(10).

We have completed our review of these applications, and they are approved, effective on the date of this letter.

As agreed to by Ms. Mary Konkowski, the following revisions will be made.

1. In the **CONTRAINDICATIONS** section, revise the proposed statement (b)(4)------ (b)(4)---------- (b)(4)----- to "Solutions containing corn-derived dextrose may be contraindicated in patients with known allergy to corn or corn products."

2. In the **PRECAUTIONS** section revise the proposed statement (b)(4)---------- (b)(4)---------- ---------- ---------- ---------- ---------- (b)(4)------ to "The intravenous administration of these solutions can cause fluid and/or

solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states, or pulmonary edema; particularly in patients with renal disease, pulmonary insufficiency, and heart disease."

The final printed labeling (FPL) must be identical and include the revisions indicated above to the package insert submitted July 22, 2003. These revisions are terms of the approval of these applications.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as they are available but no more than 30 days after they are printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-678/S-014 and NDA 20-734/S-013." Approval of these submissions by FDA is not required before the labeling is used.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submissions, please provide a highlighted or marked-up copy that shows the changes that are being made.

If additional information relating to the safety or effectiveness of these drugs become available, revision of the labeling may be required.

If a letter communicating important information about these drug products (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 appropriate 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, call Ms. Lisa Malandro, Regulatory Health Project Manager, at (301) 827-7410.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Director
Division of Anesthetic, Critical Care, and Addiction Drug Products
Office of Drug Evaluation II
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/

Bob Rappaport

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