DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-582/S-031

B.Braun Medical Inc.
2525 McGaw Avenue
P.O.Box 19791
Irvine, CA 92623-9791

Attention: Pushpa Mehta, RAC
Regulatory Affairs Specialist

Dear Ms. Mehta:

Please refer to your supplemental new drug application dated August 25, 2003, received August 27, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ProcalAmine (3% amino acid and 3% glycerin injection with electrolytes).

This "Changes Being Effected" supplemental new drug application provides for revised **PRECAUTIONS** and **WARNINGS** sections of the package insert, and revised release specification and stability protocol containing a test for aluminum determination with a validated analytical method and an acceptance criterion of NMT 25 mcg/L of aluminum in accordance with the requirements of 21 CFR 201.323.

Additionally, the following revisions are made to the package insert.

1. The statements "Care should be taken to avoid circulatory overload, particularly in patients with cardiac insufficiency. Blood sugar levels should be monitored frequently in diabetic patients." are relocated from the **PRECAUTIONS** section to the **WARNINGS** section.

2. The following paragraph is added as the fifth paragraph of **General** subsection of the **PRECAUTIONS** section.

   "To minimize the risk of possible incompatibilities arising from mixing this solution with other additives that may be prescribed, the final infusate should be inspected for cloudiness or precipitation immediately after mixing, prior to administration, and periodically during administration."

3. The following subsections are added to the **PRECAUTIONS** section.

Laboratory Tests
Frequent clinical evaluation and laboratory determinations are necessary for proper monitoring during administration.

Laboratory tests should include measurement of blood sugar, electrolyte, and serum protein concentrations; kidney and liver function tests; and evaluation of acid-base balance and fluid balance. Other laboratory tests may be suggested by the patient's condition.

Drug Interactions
Administration of barbiturates, narcotics, hypnotics or systemic anesthetics should be adjusted with caution in patients also receiving magnesium-containing solutions because of an additive central depressive effect.

4. As requested in our facsimile communication dated March 17, 2000, the following revision is made to the **Pediatric Use** subsection of the **PRECAUTIONS** section.

"Safety and effectiveness of amino acid injections in pediatric patients have not been established by adequate and well-controlled studies. However, the use of amino acid injections in pediatric patients as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance is well established in the medical literature. See **WARNINGS** and **DOSAGE AND ADMINISTRATION**."

5. In accordance with the requirements of 21 CFR 201.57(f)(10)(i), a **Geriatric Use** subsection is added to the **PRECAUTIONS** section as follows.

Geriatric Use
Clinical studies of ProcalAmine did not include sufficient numbers of subjects age 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.**

6. In accordance with the requirements of 21 CFR 201.57 an **OVERDOSAGE** section is added as follows.

   "In the event of a fluid or solute overload during parenteral therapy, reevaluate the patient's condition and institute appropriate corrective treatment."

7. As requested in our facsimile communication dated March 17, 2000, the following revision is made to the **Pediatric Use** subsection of the **DOSAGE AND ADMINISTRATION** section.

   Pediatric Use
   ProcalAmine is intended for use in adults. Use of ProcalAmine in pediatric patients is governed by the same considerations that affect the use of any amino acid solution in pediatrics. The amount administered is dosed on the basis of grams of amino acids/kg of body weight/day. Two to three g/kg of body weight for infants with adequate calories are generally sufficient to satisfy protein needs and promote positive nitrogen balance. Solutions administered by peripheral vein should not exceed twice normal serum osmolarity (718 mOsmol/L).

We have completed the review of this application, and it is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted August 25, 2003.

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 it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 18-582/S-031." Approval of this submission by FDA is not required before the labeling is used.

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 reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kim Compton, Regulatory 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/

Celia Winchell
12/24/03 09:20:23 AM
for Bob A. Rappaport, M.D., Division Director