DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-355/S-004

Aventis Behring
Attention: Allyson Chambers
Associate Director, Regulatory Affairs
1020 First Avenue
P.O. Box 61501
King of Prussia, PA 19406-0901

Dear Ms. Chambers:

Please refer to your supplemental new drug application dated February 21, 2002 , received February 22, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Stimate™ (desmopressin acetate) Nasal Spray, 1.5 mg/mL.

Although you submitted this supplement as a "Special Supplement – Changes Being Effected" under 21 CFR 314.70(c), this submission did not qualify because it did not contain final printed labeling.

This supplemental new drug application provides for addition of a "Geriatric use" subsection (reproduced below) to the PRECAUTIONS section of the package insert as required by 21 CFR 201.57(f)(10)(ii)(A) and (C).

> **"Geriatric Use**: Clinical studies of Stimate™ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects. However, other post-marketing experience has reported the occurrence of hyponatremia with the use of desmopressin acetate and fluid overload.
>
> "Therefore, in elderly patients fluid intake should be adjusted downward in an effort to decrease the potential occurrence of water intoxication and hyponatremia. Particular attention should be paid to the possibility of the rare occurrence of an extreme decrease in plasma osmolality that may result in seizures, which could lead to coma.
>
> "Patients who do not have need of antidiuretic hormone for its antidiuretic effect should be cautioned to ingest only enough fluid to satisfy thirst, in an effort to decrease the potential occurrence of water intoxication and hyponatremia.
>
> "As for all patients, dosing for geriatric patients should be appropriate to their overall situation."

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted February 2002, patient package insert submitted February 2002).

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 20-355/S-004." Approval of this submission by FDA is not required before the labeling is used.

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, call Steve McCort, Regulatory Project Manager, at (301) 827-6415.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and
Endocrine Drug Products, HFD-510
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/

Eric Colman
8/21/02 02:41:23 PM
Eric Colman for David Orloff