DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

Transmitted Via Facsimile

APR 27 1999

Rosann Reinhart
Executive Director, Regulatory Affairs
Serono Laboratories, Inc.
100 Longwater Circle
Norwell, MA 02061

Re: NDA 20-604
Serostim [somatropin (rDNA origin) for injection]
MACMIS ID# 7900

Dear Ms. Reinhart:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Serostim (somatropin (rDNA origin) for injection) disseminated by Serono Laboratories, Inc. (Serono) that violate the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Reference is made to a Slim jim brochure/Sales Aid, submitted under cover of Form FDA 2253 on February 10, 1999. DDMAC has reviewed this material and has determined that it contains promotional claims that are false or misleading and lacking in fair balance. DDMAC requests that the use of the above referenced material and those containing similar promotional claims or presentations cease immediately.

On November 13, 1998, Serono submitted a proposed Sales Aid/Leave behind to DDMAC for comment pursuant to 21 CFR 314.550. On December 23, 1998, DDMAC opined that the proposed Sales Aid/Leave behind would be false, lacking in fair balance, or otherwise misleading for several reasons. All of the violative claims and/or presentations cited herein were previously communicated to Serono in the DDMAC letter dated December 23, 1998.

Misleading Efficacy Claims or Presentations

The claim "Provides evaluable results within 2 weeks" is misleading because it minimizes the importance of the usage recommendations from the INDICATIONS AND USAGE section of the approved product labeling (APL). The APL states that "[T]he continued use of Serostim treatment should be reevaluated in patients who continue to

lose weight in the first two weeks of treatment." The purpose of this recommendation is to caution against continued use of Serostim in patients who continue to lose weight at two weeks, since this weight loss may be indicative of nonresponsiveness to Serostim. This claim is misleading because it mitigates the important precaution regarding discontinuation of treatment after 2 weeks in patients who are non-responders.

Without adequate context, the claims about physical function testing results are misleading because they overstate the efficacy of Serostim. To provide context for these claims, the following information from the APL should have been presented in close proximity and with reasonably comparable prominence. The information is presented but not with a prominence and proximity that provides effective qualification of claims. The qualifying statements are separated from the physical function discussion by a solid black line and under a separate header (important safety information).

- Improvement in physical function, as indicated by treadmill performance, was significantly correlated with the increases in LBM. No such correlation was seen with body fat;

- Isometric muscle performance as measured by grip strength dynamometry declined, probably as a result of a transient increase in tissue turgor known to occur with r-hGH therapy.

The phrase, "regardless of race or gender," is misleading because it is unsubstantiated given the limited number of women studied. Only ten female patients out of a total of 205 patients were included in the pivotal studies. Of these ten females, only five, in fact, received Serostim and of these five, only one experienced an increase in body weight from baseline.

Minimizing Significance of Product Risks

The claim, "Excellent tolerability" is misleading because it implies that Serostim is better tolerated than has been demonstrated by substantial evidence. Specifically, a parameter which may be indicative of a product's tolerability is the rate at which patients drop out of a clinical trial. In the Serostim clinical trials, patients treated with Serostim dropped out of the clinical studies at a significantly higher rate than those treated with placebo. In addition, 22 adverse events occurred in the controlled trials in at least 10% of those who received Serostim, not an insignificant number. Furthermore, 16 of these adverse events occurred at a greater frequency with Serostim than in the placebo arm.

The claim, "Glucose monitoring only in patients with known risk factors" is misleading because it does not accurately present the precautionary statements regarding glucose monitoring from the APL. Since hyperglycemia may occur in HIV-infected individuals due to a variety of conditions, these patients should be monitored for development of this condition. The presentation of this precautionary statement in this manner, e.g., unqualified and under the headline "Serostim offers the following benefits", would minimize the risk for development of hyperglycemia in these patients.

Serono should immediately cease using the referenced material and all other promotional materials containing the same or similar claims and presentations. Serono should submit a written response to DDMAC, on or before May 11, 1999, describing its intent and plans to comply with the above. In its letter to DDMAC, Serono should include a list of all promotional materials that were discontinued, and the discontinuation date.

If Serono has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or in writing at DDMAC, HFD-40, Room 17B-20, 5600 Fishers Lane, Rockville MD 20857. DDMAC reminds Serono that only written communication is considered official.

In all future correspondence regarding this matter, please refer to MACMIS # 7900 and NDA 20-604.

Sincerely,

Michael A. Misocky R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications