**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-280/S-044

Pharmacia & Upjohn Company
Attention: Madeleine Jester
Director, Regulatory Affairs
235 East 42nd Street 150/7/9
New York, NY 10017

Dear Ms. Jester:

Please refer to your supplemental new drug application dated April 30, 2003, received March 5, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Genotropin (somatropin [rDNA origin] for injection).

We acknowledge receipt of your submission dated September 17, 2003.

This "Changes Being Effected" supplemental new drug application provides for labeling changes (additions) to the CONTRAINDICATIONS and WARNINGS sections of the package insert for patients with Prader-Willi Syndrome.

We completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the electronic final printed labeling submitted on April 30, 2003, with the agreed-upon revisions to the package insert (see below) per the documentation on October 28, and 29, 2003, between you and Monika Johnson of this division. These revisions can be reported to the Agency in the next annual report for this application.

**WARNINGS**

> **There have been reports of fatalities after initiating therapy with growth hormone in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnea, or unidentified respiratory infection. Male patients with one or more of these factors may be at greater risk than females. Patients with Prader-Willi syndrome should be evaluated for signs of upper airway obstruction and sleep apnea before initiation of treatment with growth hormone. If during treatment with growth hormone, patients show signs of upper airway obstruction (including onset of or increased snoring) and/or new onset sleep apnea, treatment should be interrupted. All patients with Prader-Willi syndrome treated with growth hormone should also have effective weight control and be monitored for signs of respiratory infection, which should be diagnosed as early as possible and treated aggressively (see CONTRAINDICATIONS).**

**CONTRAINDICATIONS**

**Growth hormone is contraindicated in patients with Prader- Willi syndrome who are severely obese or have severe respiratory impairment (see WARNINGS).**

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 Monika Johnson, Regulatory Project Manager, at (301) 827-9087.

Sincerely,

*{See appended electronic signature page}*

David G. Orloff, MD
Director
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation Research

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/s/
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Mary Parks
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for Dr. Orloff