**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-008/S-018, S-019

Novartis Pharmaceuticals Corporation
Attention: Lynne Fahey Mcgrath, MPH, PhD
Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Mcgrath:

Please refer to your supplemental new drug applications dated November 10, 2005, received November 10, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sandostatin (octreotide acetate for injectable suspension) LAR Depot.

We acknowledge receipt of your submissions for S-018 dated March 8, 2006, and for S-019 dated December 23, 2005.

**Supplement-018** provides the results of a study of the use of Sandostatin LAR Depot in pediatric patients with hypothalamic obesity and responds to the January 7, 2004, pediatric written request issued by the Agency. The results of the pediatric study are added to the package insert as follows.

> The CLINICAL PHARMACOLOGY (*Pharmacokinetics*) (2. *Pharmacokinetics of Sandostatin LAR Depot*) was amended with the following paragraph:
>
> **In pediatric patients with hypothalamic obesity, the mean octreotide concentration after 6 doses of 40 mg Sandostatin LAR® Depot administered by IM injection every four weeks was approximately 3.0 ng/mL. Steady-state concentration was achieved after 3 injections of 40 mg dose.**
>
> The PRECAUTIONS (*Pediatric Use*) subsection is amended with addition of the following paragraph.
>
> **The efficacy and safety of Sandostatin LAR Depot were examined in a randomized, double-blind, placebo-controlled six-month study in 60 pediatric patients aged 6 – 17 years with hypothalamic obesity resulting from cranial insult. Mean BMI increased 0.1 kg/m$^2$ in Sandostatin LAR Depot–treated subjects compared to 0.0 kg/m$^2$ in saline control-treated subjects. Diarrhea occurred in 11 of 30 (37%)**

**patients treated with Sandostatin LAR Depot. No unexpected adverse events were observed. However, with Sandostatin LAR Depot 40 mg once a month, the incidence of new cholelithiasis in this pediatric population (33%) was higher than that seen in other adult indications such as acromegaly (22%) or malignant carcinoid syndrome (24%), where Sandostatin LAR Depot dosing was 10 to 30 mg once a month.**

**Supplement-019** provides for the addition of a PRECAUTIONS (*Geriatric Use*) subsection to the package insert.

**Geriatric Use**
**Clinical studies of Sandostatin did not include sufficient numbers of subjects aged 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.**

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

Please submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDAs.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-008/S-018, S-019." Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must submit patent information on form FDA 3542, *Patent Information Submitted Upon and After Approval of an NDA or Supplement*, within 30 days of the date of this letter as required by 21 CFR 314.53(c)(2)(ii) and 314.53(d)(2) at the address provided by 21 CFR 314.53(d)(4). The form may be obtained at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html. To expedite review of this patent declaration form, we request you submit an additional copy of the form to the S-018 application and to the Center for Drug Evaluation and Research "Orange Book" staff at

Food and Drug Administration
Office of Generic Drugs, HFD-610
Orange Book Staff
7500 Standish Place
Metro Park North II
Rockville, MD 20855-2773

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert(s) directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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 Enid Galliers, Chief, Project Management Staff, at 301-796-1211.

Sincerely,

*{See appended electronic signature page}*

Mary H. Parks, M.D.
Acting Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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Mary Parks

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