NDA 19-886/S-013

December 24, 1998

Searle
Attention: Ms. Doranne Frano
Associate Director, Regulatory Affairs
4901 Searle Parkway
Skokie, IL 60077

Dear Ms. Frano:

Please refer to your supplemental new drug application dated December 22, 1997, received December 24, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Synarel (nafarelin acetate) nasal solution.

We acknowledge receipt of your submissions dated November 17, and December 3 (2), 10, 18, 21 and 22, 1998.

We also acknowledge receipt of your submission dated November 16, 1998, however this submission was not reviewed for this supplemental application.

This supplemental new drug application provides for revisions to the **CLINICAL PHARMACOLOGY** and **ADVERSE REACTIONS** sections of the Package Insert. Specifically, to add the language listed below.

CLINICAL PHARMACOLOGY section

A new sixth paragraph that reads:

> In a single controlled clinical trial, intranasal Synarel (nafarelin acetate) at a dose of 400 micrograms per day was shown to be clinically comparable to intramuscular leuprolide depot 3.75 mg monthly, for the treatment of symptoms (dysmenorrhea, dyspareunia and pelvic pain) associated with endometriosis.

ADVERSE REACTIONS section,
Changes in Bone Density subsection

Two new sentences at the beginning of paragraph two that read:

> After six months treatment with Synarel, bone mass as measured by dual x-ray bone densitometry (DEXA), decreased 3.2%. Mean total vertebral mass, re-examined by DEXA six months after completion of treatment, was 1.4% below pretreatment.

We have completed the review of this supplemental application, as amended, 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 dated December 22, 1998). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case 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 supplemental NDA 19-886/S-013." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a Dear Health Care Practitioner 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, contact Christina Kish, Project Manager, at (301) 827-4260.

Sincerely,

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research