CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-406

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-406

Unigene Laboratories, Inc.
Attention: Brenda Marczi, Pharm. D.
Senior Director, Regulatory Affairs
83 Fulton Street
Boonton, NJ 07005

Dear Dr. Marczi:

Please refer to your new drug application (NDA) dated and received March 6, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fortical [calcitonin-salmon) (rDNA origin)] Nasal Spray.

We acknowledge receipt of your submissions dated January 6 and 21, April 14, and 26, June 22, September 13, and 15, 2004, and January 28, February 7, and March 11, and 31, 2005. Your submission of September 15, 2004 constituted a complete response to our December 31, 2003, action letter.

This new drug application provides for the use of Fortical [calcitonin-salmon) (rDNA origin)] Nasal Spray for the treatment of osteoporosis in women greater than 5 years post menopause with low bone mass relative to healthy premenopausal females.

We have completed the review of this 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 application is approved effective on the date of this letter.

Sufficient stability data has been submitted to support a 24-month expiration date.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert, patient package insert, carton label, and vial label submitted March 11, 2005). 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 an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated **"FPL for approved NDA 21-406."** Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and

effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving the pediatric study requirement for this application.

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 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 Randy Hedin, R.Ph., Senior Regulatory Management Officer, at (301) 827-6392.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure