DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-185 **NDA APPROVAL**

Parexel Consulting for LEO Pharmaceuticals Products, Ltd.
Attention: Alberto Grignolo, Ph.D.
Corporate Vice President and General Manager, Drug Development Consulting
900 Chelmsford Street
Lowell, MA 01851

Dear Dr. Grignolo:

Please refer to your new drug application (NDA) dated June 19, 2007, received June 28, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TACLONEX SCALP® (calcipotriene 0.005% and betamethasone dipropionate 0.064%) Topical Suspension.

We acknowledge receipt of your submissions dated August 2 and 20, September 4 and 10, October 10, and December 10 and 14, 2007; January 22, February 7 and 18, March 12, and April 10 and 11, 2008.

This new drug application provides for the use of TACLONEX SCALP® (calcipotriene 0.005% and betamethasone dipropionate 0.064%) Topical Suspension for topical treatment of moderate to severe psoriasis vulgaris of the scalp in adults aged 18 years and above.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and text for the patient package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, designate this submission, "**SPL for approved NDA 22-185**."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).*

Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-185**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with final printed labeling (FPL) that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 months to up to 12 years because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group. Young children have greater surface-area-to-volume ratios, which increase the risk of hypothalamic-pituitary-adrenal axis suppression associated with the use of a drug product which contains a potent corticosteroid.

We are deferring submission of your pediatric study for ages 12 to 17 years for this application until September 2012 because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This required study is listed below.

1. Conduct a study in pediatric patients ages 12 to 17 years of TACLONEX SCALP® Topical Suspension for the treatment of scalp psoriasis. Enrollment should be sufficient to allow for 100 evaluable patients. Evaluate the effect of TACLONEX SCALP® Topical Suspension on calcium metabolism in all subjects and on the hypothalamic-pituitary axis in a subset of 30 patients.

   Final Report Submission: September 2012

Submit the final study report to your NDA 22-185. Use the following designator to prominently label all submissions related to this pediatric study:

- **Required Pediatric Assessment**

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain

purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)). This provision took effect on March 25, 2008.

Based on appropriate scientific data consistent with ICH Guidelines, FDA has determined that you are required to conduct the following nonclinical postmarketing study to identify whether TACLONEX SCALP® Topical Suspension is associated with the unexpected serious risk of cancer. See *The Need for Long-Term Rodent Carcinogenicity Studies of Pharmaceuticals*, ICH-S1A (March 1996).

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify the potential of calcipotriene to cause cancer. Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and would not be sufficient to identify the potential of calcipotriene to cause cancer.

Therefore, FDA has determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct the following postmarketing study:

1. Evaluate the carcinogenic potential of calcipotriene in a two-year oral study in rats.

The timetable you submitted on April 11, 2008, states that you will conduct this study according to the following timetable:

Protocol Submission:	December 2008
Study Start Date:	September 2009
Final Report Submission:	September 2012

Submit the nonclinical protocol to your IND 67,835, with a cross-reference letter to this NDA 22-185. Submit all final reports to your NDA 22-185. Use the following designators to prominently label all submissions, including supplements, relating to this postmarketing study as appropriate:

- **Required Postmarketing Protocol under 505(o)**
- **Required Postmarketing Final Report under 505(o)**
- **Required Postmarketing Correspondence under 505(o)**

You are required to report periodically to FDA on the status of this postmarketing study pursuant to sections 505(o)(3)(E)(ii) and 506B of the FDCA, as well as 21 CFR 314.81. Under section 505(o)(3)(E)(ii), you are also required to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue associated with TACLONEX SCALP® Topical Suspension.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package inserts to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

If you have any questions, call Melinda Bauerlien, M.S., Regulatory Project Manager, at (301) 796-0906.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, M.D., F.A.A.D.
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Stanka Kukich
5/9/2008 03:57:16 PM
sign off for Dr. Susan Walker, Division Director