DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021359

**NDA APPROVAL**

ProStrakan, Inc.
1430 US Highway 206, Suite 110
Bedminster, NJ 07921-2652

Attention: Dalena DeGrezia, MBA
Director, US Regulatory Affairs

Dear Ms. DeGrezia:

Please refer to your New Drug Application (NDA) dated June 22, 2001, withdrawn April 25, 2002, resubmitted June 30, 2004, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for RECTIV (nitroglycerin) Ointment 0.4%.

We acknowledge receipt of your amendments dated August 8, October 24, November 16, 21, and 27, and December 17, 2001, January 4, 22, and 31, February 6, and April 24 and 29, 2002, September 3, 21, 28, and 30, October 5, 6, 22, and 26, November 3 and 19, and December 14, 21 (2), 22, and 23, 2004, April 14, 2005, May 22, July 10, and December 12, 2006, January 29, 2008, January 9, and September 30 (2), 2009, January 14, March 10 and 17, July 9, and December 20, 2010, March 22, April 7, May 5, 6, 20, and 26, and June 16, 2011.

The December 20, 2010, submission constituted a complete response to our March 30, 2010, action letter.

This new drug application provides for the use of RECTIV (nitroglycerin) Ointment 0.4% for the treatment of moderate to severe pain associated with chronic anal fissure.

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, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert and text for the patient package insert. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## 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 (June 2008)." 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 021359**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with 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 month to 1 month because necessary studies are impossible or highly impracticable. This is because the condition does not exist in this population.

We are deferring submission of your pediatric study for ages 1 month to 16 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are 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 Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1791-1 Multiple-dose pharmacokinetics study of 0.4% nitroglycerin ointment in subjects ≥12 years to <17 years, in order to determine the appropriate doses for efficacy and safety evaluations.

Final Protocol Submission: January 2012
Study/Trial Completion: June 2013
Final Report Submission: December 2013

1791-2 Multiple-dose pharmacokinetics study of 0.4% nitroglycerin ointment in subjects ≥1 month to <12 years, in order to determine the appropriate doses for efficacy and safety evaluations.

Final Protocol Submission: January 2012
Study/Trial Completion: June 2013
Final Report Submission: December 2013

1791-3 Safety, efficacy, and pharmacokinetics study in subjects ≥12 years to <17 years.

Final Protocol Submission: June 2013
Study/Trial Completion: June 2015
Final Report Submission: December 2015

1791-4 Safety, efficacy, and pharmacokinetics study in subjects ≥3 years to <12 years.

Final Protocol Submission: June 2013
Study/Trial Completion: June 2015
Final Report Submission: December 2015

1791-5 Safety and pharmacokinetic study in subjects ≥1 month to <3 years.

Final Protocol Submission: June 2013
Study/Trial Completion: June 2015
Final Report Submission: December 2015

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

**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 insert 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 http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

**EXPIRATION DATING PERIOD**

A shelf life of 18 months has been granted for the drug product when stored under the labeled conditions of 20°-25°C (68°-77°F); excursions permitted between 15°-30°C (59°-86°F).

**REPORTING REQUIREMENTS**

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 Christopher Hilfiger, Regulatory Project Manager, at (301) 796-4131.

Sincerely,

*{See appended electronic signature page}*

Rigoberto Roca, MD
Deputy Director
Division of Anesthesia, Analgesia,
and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

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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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RIGOBERTO A ROCA
06/21/2011