DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-789

Dow Pharmaceutical Sciences
Attention: Barry M. Calvarese, MS
Vice President Regulatory and Clinical Affairs
1330 Redwood Way
Petaluma, CA 94954-1169

Dear Mr. Calvarese:

Please refer to your new drug application (NDA) dated August 27, 2004, received August 30, 2004, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for METROGEL (metronidazole gel), 1%.

We acknowledge receipt of your submissions dated September 3 and 28, October 22, November 11, December 28, 2004; February 7 and 14, March 8, 23 and 29, April 12, 21 and 26, June 13, 23 and 24 (2), 2005, and facsimile of June 27 and 29, 2005.

This new drug application provides for the use of METROGEL (metronidazole gel), 1% for the topical treatment of inflammatory lesions of rosacea.

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

We concur with your commitment to revise the carton and container label as per your amendment received via facsimile dated June 27, 2005, and further agreed upon via teleconference on June 29, 2005. The final printed proprietary name on the carton and container must be identical to the proprietary name on the enclosed labeling.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert). 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, designate this submission "**FPL for approved NDA 21-789**." 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.

We remind you of your post-marketing commitments dated June 27 and 29, 2005, received via facsimile in which you agreed to the following:

Clinical:

- To conduct a long term safety study of one year duration in at least 100 evaluable patients with rosacea, to include quarterly complete blood counts with differential, and assessment for local safety and adverse events.

  Protocol Submission: **January 30, 2006**

  Study Start: **June 30, 2006**

  Final Report submissions: **June 30, 2008**

Chemistry, Manufacturing and Controls:

- To submit a Labeling Supplement for carton and container product nomenclature to be printed as METROGEL® (metronidazole gel), 1%, before the current supply of the carton and container printed as METROGEL® 1% (metronidazole) gel 1%, is exhausted. Printing of the revised carton and container labels should not be initiated until format and content are agreed upon and the supplement approved.

  Submit Labeling Supplement for a revised carton and container no later than December 31, 2005.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

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, the Division of Dermatologic & Dental Drug Products, 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, MD 20857

Please submit one market package of the drug product when it is available.

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, please call Kalyani Bhatt, 301-827-2020.

Sincerely,

{See appended electronic signature page}

Jonathan Wilkin, MD
Division Director,
Division of Dermatologic & Dental Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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
6/30/05 05:42:03 PM
sign off for Dr. Jonathan Wilkin, Division Director