CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-586

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-586

3M Health Care
Attention: Suzanne M. Danielson, RAC
Director of Regulatory Affairs and Quality
3M Center, Building 275-5W-06
St. Paul, MN 55144-1000

Dear Ms. Danielson:

Please refer to your new drug application (NDA) dated October 24, 2003, received October 27, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for DuraPrep™ Surgical (iodine povacrylex and 74% isopropyl alcohol) Solution.

We acknowledge receipt of your submissions dated October 29, 2003; February 23, March 9 and 16, April 20, June 24, and August 11, 12 and 19 (2), 2004.

We completed our review of this application, as amended, and it is approvable. The primary deficiency in this application is that the data provided failed to demonstrate that DuraPrep Surgical Solution achieves the expected mean three $\log_{10}$ reduction of bacterial counts in the groin at ten minutes after application. Further, we have concluded that the additional data provided, including the comparisons between DuraPrep and the positive control in the two Phase 3 studies and the bacterial challenge studies, are not adequate to support a conclusion that the product is effective for its intended use.

Before the application may be approved it will be necessary for you to conduct a clinical study in which a mean three $\log_{10}$ reduction in skin flora on the groin at 10 minutes post application is demonstrated for DuraPrep™ Surgical Solution. This study should be designed as recommended in the FDA Proposed Tentative Final Monograph (TFM) for Health Care Antiseptic Drug Products, Effectiveness Testing of a Patient Preoperative Skin Preparation, published in the Federal Register on June 17, 1994. The study should include an appropriate active control and a treatment arm using DuraPrep solution that does not contain iodine. You are strongly encouraged to consult the Division of Anti-Infective Drug Products and the Division of Over-the-Counter Drug Products regarding the design of the new study prior to initiation.

Further revisions to the draft labeling will be necessary pending the submission and review of the data from the requested clinical study. We appreciate your continued willingness to work with the Agency to resolve all outstanding labeling issues.

In addition, we remind you of the following agreements made during the August 19, 2004 teleconference between representatives from 3M and the FDA.

Chemistry

1. Obtain guidance in selecting an established name that describes your product from the U.S. Adopted Names Council (USAN). Submit a copy of your USAN paperwork and application to this NDA on or before September 1, 2004. (Refer to 21 CFR. 299.4.)

2. Use the established name "iodine povacrylex" until USAN determines an acceptable established name for your product.

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

   - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
   - Present tabulations of the new safety data combined with the original NDA data.
   - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
   - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.

5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

7. Provide English translations of current approved foreign labeling not previously submitted.

In addition, we request that you submit two copies of the introductory promotional materials you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Please send one of the copies to the Division of Anti-Infective Drug Products and the other copy, along with the labeling, to Division of Over-the-Counter Drug Products, HFD-560.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division of Anti-Infective Drug Products and the Division of Over-the-Counter Drug Products to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Maureen Dillon-Parker, Regulatory Project Manager, at (301) 827-2125.

Sincerely,

{See appended electronic signature page}

John K. Jenkins, M.D.
Director
Office of New Drugs
Center for Drug Evaluation and Research

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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.

/s/

John Jenkins
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