DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administr
Rockville MD 20857

NDA 21-026

Johnson & Johnson Consumer companies, Inc.
Attention: Paul F. Manley
Director, Drug Regulatory Affairs
199 Grandview Road
Skillman, New Jersey 08558-9418

JUN 28 1999

Dear Mr. Manley:

Please refer to your new drug application (NDA) dated August 24, 1998, received August 24, 1998, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pediastat (miconazole nitrate) Diaper Rash Ointment, 0.25%.

We acknowledge receipt of your submissions dated October 6, November 18, and November 20, 1998; January 7, March 1, March 30, and May 25, 1999.

We have completed our review and find the information presented is inadequate, and the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

CLINICAL:

1. The indication requires clear-cut definition so that the product may be recommended for a target population who can receive the clinical benefit without introducing the risk of drug resistance through indiscriminate use. An indication for the treatment of moderate or severe diaper dermatitis in association with *C. albicans infection* in infants may be acceptable, if a clinical trial, in which the severity of disease is properly defined and *C. albicans* infection is demonstrated both by wet mount examination of pseudohyphae and by culture, shows superiority of miconazole nitrate, 0.25% ,ointment over the ointment base.

2. Any planned clinical trial should have sufficient representation from both sexes and from minorities to permit proper subset analysis.

3. The possibility of adverse effect by the ointment base should be addressed in a 3-arm study which includes a treatment group not exposed to the ointment base.

4. The relevance of the dermal safety studies should be addressed, especially with respect to (i) target population being infants and not adults, (ii) test sites not in diaper area, and (iii) appropriateness of using UVA alone in phototoxicity testing and in the challenge phase of the photoallergenicity study.

CHEMISTRY:

1. During recent inspections of the manufacturing facilities for your NDA, a number of deficiencies were noted and conveyed to you or your suppliers by the inspector. Satisfactory inspections will be required before this application may be approved.

2. The release testing program is unacceptable in that:
   a. degradation testing must be included in the release testing program,
   b. the Appearance, Odor, and Weight tests, as well as the ZnO ID and assay tests, must should be part of the release testing program,
   c. the ID test for miconazole nitrate should be changed to USP <197> or <201>,
   d. the batch sampling plan is unacceptable. Every batch lot must meet its analytical specifications via testing (c.f., 21 CFR 211.165).

3. Please verify that no reprocessing of the drug product will occur under any circumstances.

Although not the basis for the non approval of this application, the following information is requested:

1. The procedure to determine
   Please submit the exact test method or SOP to measure . Alternately, the compendial method may be used.

2. The nature of the is not specified; it is, however, stated that the is acceptable for food-contact use. More information about the is required, specifically, its chemical composition.

3. You have not specified the humidity at which the accelerated stability data were obtained. Also, storage conditions were stated to be below 30°C, but should probably be restated to indicate: Store at room temperature.

4. The tradename, Pediastat, was found unacceptable. The principal reason was that the suffix "stat" implied fast-acting.

5. If an OTC Final Monograph for Diaper Rash that includes zinc oxide as active ingredient is published, contribution of therapeutic effect by zinc oxide may need to be demonstrated.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. 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.

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, contact Millie Wright, Project Manager, at (301) 827-2020.

Sincerely,

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research