NDA 21-108

Johnson and Johnson Consumer Companies, Inc.
Attention: Kathleen Wille, Ph.D., Manager, Regulatory Affairs
199 Grandview Road
Skillman, NJ 08558-9418

Dear Dr. Wille:

Please refer to your new drug application (NDA) dated August 31, 1999, received September 1, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for RENOVA® (tretinoin cream), 0.02%.

We acknowledge receipt of your submissions dated September 23, October 13 and 25, December 16 and 20, 1999; February 29, March 17, April 4 and 27, June 7, 15(two) and 23, July 7 and 17, August 30(facsimile) and 31(2 facsimiles), 2000.

This new drug application provides for the use of RENOVA® (tretinoin cream), 0.02%, for the mitigation (palliation) of fine facial wrinkles in patients who use comprehensive skin care and sunlight avoidance programs.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text with revisions listed in the facsimile of your letter dated August 31, 2000, regarding the carton and container labeling. These revisions are listed below. Accordingly, the application is approved effective on the date of this letter.

1. The drug name and strength will be represented in a typeface identical to the brand name in design and boldness, and the drug name and strength are no smaller than half the size of the brand name on both the container and the carton.

2. The use of the contrasting colors to differentiate RENOVA® (tretinoin cream), 0.02%, and RENOVA® (tretinoin cream), 0.05%.

3. The carton and container label will portray “For Topical Use Only”, coupled with full instructions described in the package insert.

4. The “Rx Only” will be relocated in the principal display panel.

5. The statements: “New Strength” and “New Formula” will be used for a period not to exceed six months.

6. The storage statement on the carton will be consistent with FDA approved storage statement in the package insert.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). 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 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-108." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in the facsimile of your letters dated August 31, 2000. These commitments, along with any completion dates agreed upon, are listed below:

1. Your commitment to provide the UV-VIS spectra, from 200 to 700 nm, for the individual components of the drug product and the drug product itself within 30 days of approval.

2. Your commitment to conduct one comparative efficacy (in fine wrinkling only) and safety study between RENOVA® (tretinoin cream), 0.02%, and the currently marketed RENOVA® (tretinoin cream) 0.05%, (TEC-IA). The protocol will be submitted within 6 months of approval and the results of this study will be submitted to the Agency within 3 ½ years of approval. No comparisons between RENOVA® (tretinoin cream), 0.02%, and the previously marketed RENOVA® (tretinoin cream), 0.05%, will be made with regard to efficacy or safety without this study.

3. Your commitment to submit the results of the currently ongoing RENOVA (TEC-IA) 0.05% Phase 4 study in non-Caucasians to demonstrate local intolerance in Asian and Hispanic skin. The demographics will be adequately representative of the Asian and Hispanic demographics as reported in the year 2000 United States Census. Results of this study will be submitted to the Agency within 3 ½ years of approval.

4. Your commitment to conduct a UV analysis of the new/different components of the RENOVA (TEC II) 0.02% formulation versus the RENOVA (TEC-IA) 0.05% formulation. If the new ingredients in the RENOVA (TEC II) 0.02% contribute to the UVA, UVB, and visible absorption, you are committed to conduct a Phase 4 study to evaluate the phototoxicity and photosensitizing nature of the fragranced RENOVA (TECII) 0.02%. The results of this study will be reported to the Agency within 9 months of approval.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including

labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application for the indication of mitigation (palliation) of fine facial wrinkles, because this indication is unlikely to be widely seen in the pediatric population.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division 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, Maryland 20857

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Olga I. Cintron, R.Ph., Project Manager, at (301) 827-2020.

Sincerely yours,

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