CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-502

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-502

L'Oreal USA Products, Inc.
Attention: Jean R. Grieve
Assistant Vice President, Drug Approval Group
30 L'Oreal Way
Clark, NJ 07066

Dear Ms. Grieve:

Please refer to your new drug application (NDA) dated May 12, 2005 received May 12, 2005, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Anthelios SX (2% avobenzone, 2% ecamsule, and 10% octocrylene) cream distributed by LaRoche-Posay.

We acknowledge receipt of your submissions dated April 12, May 18, June 22 and 23, and July 10, 12, and 20, 2006.

The May 18, 2006 submission constituted a complete response to our March 10, 2006 action letter.

This new drug application is indicated to help the prevention of sunburn and to help provide protection from UVA and UVB rays.

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 agreed-upon labeling text and with the minor editorial revisions listed below.

1. Replace "[illegible]" with "wavelengths" in every occurrence on the labels.
2. Remove [illegible] from the third bulleted statement under ***Uses*** so that it reads, "helps provide protection from UVA rays (short and long wavelengths)."

The final printed labeling (FPL) must be identical to, except for including the revisions listed, the enclosed labeling (immediate carton and container labels submitted July 20, 2006), and must be in the "Drug Facts" format (21 CFR 201.66). These revisions are terms of the NDA approval for the 3.4 oz. (100 g) product. Marketing the product before making the revisions, exactly as stated, in the product's labeling and in the required format 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 these submissions "**FPL for approved NDA 21-502**." Approval of this submission by FDA is not required before the labeling is used.

[redacted] If you intend to market this product under additional labeling (e.g., under a different trade name) or increase the package size from 3.4 oz. (100 g), you must submit a prior approval supplement.

The Agency is evaluating further the appropriate labeling statements for OTC sunscreen drug products. We will inform you of any additional changes to the labeling of these products that the Agency deems necessary in the future.

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 deferring submission of your pediatric studies for under the age of 6 months until July 22, 2009.

Your deferred pediatric study required under section 2 of the Pediatric Research Equity Act (PREA) is considered a required postmarketing study commitment. The status of this postmarketing study shall be reported annually for each NDA according to 21 CFR 314.81. This commitment is listed below.

1. Deferred pediatric study under PREA for the prevention of sunburn in pediatric patients under the age of 6 months.

   Final Report Submission: July 22, 2009

Submit final study reports to NDA 21-502. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 796-0843.

Sincerely,

{See appended electronic signature page}

Charles Ganley, M.D.
Director
Office of Nonprescription Products
Center for Drug Evaluation and Research

Sincerely,

{See appended electronic signature page}

Julie Beitz, M.D.
Acting Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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L'Oreal USA Products, Inc.
Attention: Jean R. Grieve
Assistant Vice President, Drug Approval Group
30 L'Oreal Way
Clark, NJ 07066

Dear Ms. Grieve:

Please refer to your new drug applications (NDA) dated May 12, 2005 received May 12, 2005 (NDA 21-502) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for 2% avobenzone, 2% ecamsule, and 10% octocrylene cream (NDA 21-502).

These products are indicated for the prevention of sunburn.

We acknowledge receipt of your submissions dated August 5, September 8 (NDA 21-502) and December 19, 2005, and January 11, February 16 (NDA 21-502).

We have completed our review of these applications, as amended, and they are approvable. Before these applications may be approved, however, you must submit draft labeling revised as follows:

1. Make the changes described below to labeling *inside* the Drug Facts box. Unless otherwise specified, the changes apply to all products

2 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Approvable Letter- 14

Before these applications may be approved, FDA must conduct an inspection of the manufacturing facilities referenced in the applications to determine satisfactory compliance with cGMPs. The cGMP inspection for a facility which manufactures one of the drug substances has not been completed as of this date.

In addition, we are still reviewing the multiple trade names for your formulations.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

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.

Within 10 days after the date of this letter, you are required to amend these applications, 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 these applications 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.

These drug products may not be legally marketed until you have been notified in writing that these applications are approved.

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 796-0843.

Sincerely,

{See appended electronic signature page}

Charles Ganley, M.D.
Director
Office of Nonprescription Products
Center for Drug Evaluation and Research

Sincerely,

{See appended electronic signature page}

Julie Beitz, M.D.
Acting Director
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
3/9/2006 05:01:50 PM
Signing off for Dr. Julie Beitz, Acting Director Office of Drug Evaluation III

Andrea Segal
3/10/2006 09:33:57 AM
I am signing on behalf of Dr. Charles Ganley.