

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-502

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

L'ORÉAL
U S A

NEW CORRESP

N-000 C

DUPLICATE

RECEIVED

OCT 26 2005

CDR / CDER

October 25, 2005

Re: PATENT INFORMATION

NDA 21-502 (User Fee Id #4690)

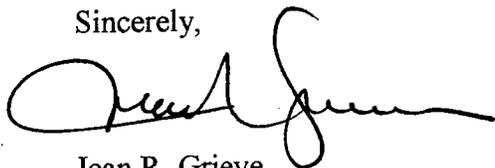
☪ ☪ ☪ SPF 15 Daily Use Moisturizing Sunscreen Lotion

Central Document Room
Center for Drug Evaluation and Research
Food & Drug Administration
5901 Unit B, Ammendale Road
Beltsville, MD 20705-1266

To Whom It May Concern:

In accordance with 21 CFR §314.53(d), L'Oreal USA Products, Inc. herewith submits the required patent information for NDA 21-502. This information is a duplicate of the information contained in Item 13 of the NDA submission. As required by 21 CFR §314.53(d), this information is being submitted in duplicate by letter, separate from the NDA submission. The original NDA was submitted to the FDA on May 12, 2005. Patent information on the correct form, FDA 3542a, was submitted to the NDA via S-003 on October 5, 2005.

Sincerely,



Jean R. Grieve
Assistant Vice President
Research & Development – Drug Approval Group
L'Oreal USA Products, Inc.

NDA No. 21-502

**ITEM 13: SUBMISSION OF PATENT INFORMATION ON ANY
PATENT WHICH CLAIMS THE DRUG (21 U.S.C. § 355 (b) or (c))**

The following information is submitted pursuant to 21 C.F.R. §314.50(h) and §314.53(c):

See Attached Forms FDA 3542a for patent 4,585,597 and patent 5,587,150.

The following information is submitted pursuant to 21 C.F.R. § 314.50(j):

I. Claimed Exclusivity (21 C.F.R. § 314.50 (j)):

- (1) Applicant L'Oréal USA Products claims five (5) years marketing exclusivity upon approval of the drug product that is the subject of this New Drug Application submitted pursuant to § 505(b) of the FD&C Act.
- (2) Applicant refers to 21 C.F.R. § 314.108(b)(2) in support of this claim.
- (3) Applicant, owner of the Mexoryl® new chemical entity '597 patent, certifies that to the best of its knowledge, a drug has not previously been approved under § 505(b) of the FD&C Act containing this NCE. *

Date:

Signed: 

ALAN J. MEYERS
Senior Vice President
Research & Development
L'Oréal USA Products
111 L'Oréal Way
Clark, NJ 07066

*The applicant has pending NDA applications on file with the Food & Drug Administration which contain this Mexoryl® new chemical entity '597 patent, a UV filter.

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT
For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

NDA NUMBER
21-502
NAME OF APPLICANT / NDA HOLDER
L'Oréal USA Products Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ACTIVE INGREDIENT(S)	STRENGTH(S)
ecamsule	2%
avobenzene	2%
octocrylene	10%

RECEIVED

OCT 26 2005

CDR / CDER

DOSAGE FORM
Topical lotion

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1 GENERAL

a. United States Patent Number 4,585,597	b. Issue Date of Patent April 29, 1986	c. Expiration Date of Patent 6/16/2005*
d. Name of Patent Owner L'Oréal S.A.	Address (of Patent Owner) River Plaza - 29, Quai Aulagnier	
	City/State Asnieres	
	ZIP Code 92600	FAX Number (if available)
	Telephone Number 331-47-56-88-03	E-Mail Address (if available) lmszputen@rd.loreal.com
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) Norman H. Stepno, Esquire Stepno, Doane, Swecker & Mathias LLP	Address (of agent or representative named in 1.e.) PO Box 1404 1737 King St.- Suite 500	
	City/State Alexandria, VA	
	ZIP Code 22314-2727	FAX Number (if available)
	Telephone Number 703-836-6620	E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

71,000,000,000

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

N/A

Yes

No

***Refers to Section 1.c.**

An application for interim patent extension under 35 U.S.C. §156 (d) (5) is currently pending before the U.S. Patent and Trademark Office.

**Appears This Way
On Original**

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? [X] Yes [] No

Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? [] Yes [X] No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). N/A [] Yes [] No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3. N/A

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) [] Yes [X] No

2.6 Does the patent claim only an intermediate? [] Yes [X] No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) N/A [] Yes [] No

3. Drug Product (Composition/Formulation)

Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? [X] Yes [] No

3.2 Does the patent claim only an intermediate? [] Yes [X] No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) N/A [] Yes [] No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? [X] Yes [] No

4.2 Patent Claim Number (as listed in the patent) 13 Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? [X] Yes [] No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Sunscreen : "For protecting human epidermis against UV-A and/or UV-B rays"

5. No Relevant Patents

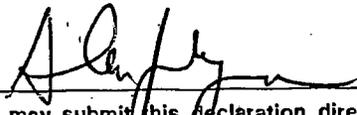
For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), a product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. [] Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and my submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below) **Date Signed**



10/5/05

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input checked="" type="checkbox"/> NDA Applicant/Holder	<input type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Alan J. Meyers	
Address L'Oréal USA Products Inc. 111 Terminal Ave	City/State Clark, NJ
ZIP Code 07066	Telephone Number 732-680-5708
FAX Number (if available) (732) 396-7051	E-Mail Address (if available) ameyers@rd.us.loreal.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
 CDER (HFD-007)
 5600 Fishers Lane
 Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

21-502

NAME OF APPLICANT / NDA HOLDER

L'Oreal USA Products Inc.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ACTIVE INGREDIENT(S)

Ecamsule
Avobenzone
Octocrylene

STRENGTH(S)

2%
2%
10%

DOSAGE FORM

Topical lotion

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

I. GENERAL

a. United States Patent Number
5,587,150

b. Issue Date of Patent
12/24/1996

c. Expiration Date of Patent
12/24/2013

d. Name of Patent Owner
L'OREAL S.A

Address (of Patent Owner)
River Plaza, 29, Quai Aulagnier

City/State
Asnieres

ZIP Code
92600

FAX Number (if available)

Telephone Number
331 47 56 88 03

E-Mail Address (if available)
lmiszputen@rd.loreal.com

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)
111 Terminal Avenue

City/State
Clark, NJ

ZIP Code
07066

FAX Number (if available)
732-396-7051

Telephone Number
732-680-5708

E-Mail Address (if available)
ameyers@rd.us.loreal.com

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

9. If the patent referenced above has
date a new expiration date?

N/A

Yes

No

Appears This Way
On Original

Appears This Way
On Original

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). N/A Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) N/A Yes No

3. Drug Product (Composition/Formulation)

Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) N/A Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Patent Claim Number (as listed in the patent) 15, 31 Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Sunscreen "Method for protecting human epidermis against UV wavelengths between 280 and 380 nm"

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in manufacture, use, or sale of the drug product. Yes

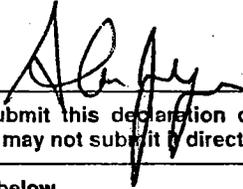
6 Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



10/5/05

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Alan J. Meyers

Address

L'OREAL USA Products Inc.
111 Terminal Avenue

City/State

Clark, NJ

ZIP Code

07066

Telephone Number

732-680-5708

FAX Number (if available)

732-396-7051

E-Mail Address (if available)

ameyers@rd.us.loreal.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

L'ORÉAL USA

Re: **NDA 21-502 - Pending Application; S-003**
☐ ☐ SPF 15 Daily Use Moisturizing Sunscreen Lotion
Item 13, Forms 3542a

October 5, 2005

Charles Ganley, M.D.
Director, Office of Nonprescription Drug Products; HFD-105
Division of Nonprescription Clinical Evaluation
Central Document Room
Food & Drug Administration
5901 Unit B, Ammendale Road
Beltsville, MD 20705

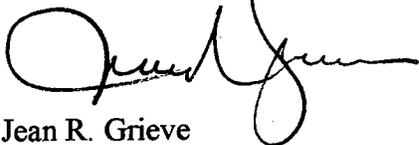
Dear Dr. Ganley:

With reference to our pending NDA 21-502 for SPF 15 Daily Use Moisturizing Sunscreen Lotion, L'OREAL USA Products, Inc. herewith submits additional information for inclusion in Item 13, Patent Information. Attached you will find one copy of Form 3542a each for patent # 4,585,597 and for patent # 5,587,150, in addition to a statement of Claimed Exclusivity pursuant to 21 CFR § 314.50(j) for the above-referenced pending NDA. This submission corrects the error in submission format and utilizes the correct FDA forms; the content of the information was included in text format in the original application. We thank you for bringing this matter to our attention.

Please do not hesitate to contact me if clarification is required.

Respectfully submitted,

L'OREAL USA Products Inc.



Jean R. Grieve
Assistant Vice President - Drug Approval Group
Research & Development division
732-680-5562

cc: Ms. E. Abraham, Project Manager, no attachments. Via fax.

RECEIVED

OCT 07 2005

ODF ORDER

N-000(c)

NEW CORRESP

DUPLICATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**

(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER
21-502

APPLICANT INFORMATION

NAME OF APPLICANT L'Oréal USA Products, Inc.	DATE OF SUBMISSION 10/5/05
TELEPHONE NO. (Include Area Code) (732) 680-5708	FACSIMILE (FAX) Number (Include Area Code) (732) 396-7051
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 111 L'Oréal Way Clark, New Jersey 07066	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Jean R. Grieve 30 L'Oréal Way Clark, New Jersey 07066 Tel: (732) 680-5562 Fax (732-909-2007) (732) 680-5502

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)	
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Association of Ecamsule (E), Avobenzone (A) USP, and Octocrylene (O) USP	PROPRIETARY NAME (trade name) IF ANY VARIOUS
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) Ecamsule: (±)(3E,3'E)-3,3'-(p-phenylenedimethylidene)bis[2-oxo-10-boranesulfonic acid	CODE NAME (If any) Daily Use Lotion
DOSAGE FORM: Lotion	STRENGTHS: E 2%, A 2%, O 10%
ROUTE OF ADMINISTRATION Topical to the Skin	

(PROPOSED) INDICATION(S) FOR USE:

Prevention of sunburn ultraviolet radiation (UVR)

OCT 07 2005
CDER/CDER

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY CBE CBE-30 Prior Approval (PA)

REASON FOR SUBMISSION

Patent Information

PROPOSED MARKETING STATUS (check one) PRESCRIPTION PRODUCT (Rx) OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS PAPER PAPER AND ELECTRONIC ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

DUPLICATE

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

This application contains the following items: (Check all that apply)	
<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling (check one) <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input checked="" type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

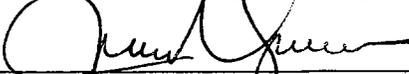
1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT



TYPED NAME AND TITLE

Jean R. Grieve
Assistant Vice President, Drug Approval Group

DATE:

10/5/05

ADDRESS (Street, City, State, and ZIP Code)

30 L'Oréal Way - Clark, New Jersey 07066

Telephone Number

(732) 680-5562

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

EXCLUSIVITY SUMMARY

NDA # 21-502

SUPPL #

HFD # 560

Trade Name Anthelios SX

Generic Name ecamsule/avobenzone/octocrylene

Applicant Name L'Oreal

Approval Date, If Known July 21, 2006

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20-045 Shade UVAguard (avobenzone)

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

— .820.01, C — — 910.01, — 920.01

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

— 820.01, [, — 910.01, — 920.01

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
IND # 59,126 YES ! NO
! Explain:

Investigation #2 !
IND # 59,126 YES ! NO
! Explain:
note: L'Oreal conducted all of the essential studies

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES

Explain:

!

!

! NO

! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Elaine Abraham

Title: RPM

Date: 7/19/06

Name of Office/Division Director signing form:

Title:

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

DEBARMENT CERTIFICATION STATEMENT (ITEM 16)

L'Oréal USA Products, Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this New Drug Application.

April 25, 2005
(Date)

Jean Grieve
(Signature)

Jean Grieve
Assistant Vice President
Drug Approval Group
L'Oréal USA Products, Inc.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NA/BLA #: 21-502 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: May 12, 2005 Action Date: _____

HFD-560 _____ Trade and generic names/dosage form: avobenzon, ecamsule, and octocrylene cream

Applicant: L'Oreal USA Products, Inc. Therapeutic Class: Sunscreen

Indication(s) previously approved: None

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Prevention of sunburn

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- X No: Please check all that apply: Partial Waiver X Deferred X Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

udies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. ≤ 6 mos. Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: Condition occurs in this population

Date studies are due (mm/dd/yy): _____ ?

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. ≥ 6 mos. Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA _____
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

ITEM 18

NDA 21-502

USER Fee # 4690

SPF 15 Daily Use Sunscreen Lotion

Attached please find two User Fee Cover Sheets and corresponding copies of checks sent to:

U.S. Food and Drug Administration
Mellon Client Service Center RM 670
500 Ross Street
Pittsburgh, PA 15262-0001

The cumulative total of these checks yields the User Fee amount of \$672,000.00, the fee rate for fiscal year 2005 for New Drug Application requiring clinical data.

1 st Check December 18, 2003 (equal to Fiscal 2004 User Fee)	\$ 573,500.00
2 nd Check December 7, 2004 (increase in User Fee for Fiscal 2005)	<u>\$ 98,500.00</u>
Total Paid	
Fiscal 2005 User Fee	\$672,000.00

PRESCRIPTION DRUG USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS L'ORÉAL SA L'ORÉAL USA Products Inc. (Official agent for L'ORÉAL SA) 30 Terminal Ave CLARK, NJ 07066	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER NO 21502
2. TELEPHONE NUMBER (Include Area Code) (732) 680-5562	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: <u>Note: NDA User Fee Payment</u> (APPLICATION NO. CONTAINING THE DATA).
3. PRODUCT NAME MEXORYL [®] SX 15 (ecamsule)	6. USER FEE I.D. NUMBER 4690

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/82 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See Item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 738(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See Item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

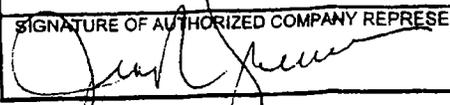
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER, HFD-94
and 12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Assistant Vice President Drug Approval group	DATE 12/19/03
---	--	------------------

105245

U.S. FOOD AND DRUG ADMIN.

CHECK NUMBER

DATE
12/18/03

Invoice No.	Description	Date	P.O. No.	Gross Amount	Discount	Net Amount
121603USF5735000	NDA21502	12/16/03		\$573,500.00	\$0.00	\$573,500.00
TOTALS:				\$573,500.00	\$0.00	\$573,500.00

[]

Mecoryll SA 15 (capsule)
NDA User Fee Payment

L'OREAL USA, INC.

PLEASE DETACH THIS REMITTANCE ADVICE BEFORE DEPOSITING CHECK

L'ORÉAL USA, Inc.

CLARK, NJ 07066

(on behalf of L'OREAL SA France)

RESEARCH & DEVELOPM

CHASE MANHATTAN BANK USA, N.A.
1201 MARKET STREET
WILMINGTON, DE 19801

62-26 80544
311

NO.

DATE 12/18/03

CHECK NO

AMOUNT
\$ *****573,500.00

PAY FIVE HUNDRED SEVENTY THREE THOUSAND FIVE HUNDRED DOLLARS AND 00 CENTS

Dollars

PAY
TO THE
ORDER
OF

U.S. FOOD AND DRUG ADMIN.
PO BOX 360909
PITTSBURGH PA 15251-6909

NDA Number N21502
User Fee ID Number 4690

AUTHORIZED SIGNATURE

PRESCRIPTION DRUG USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS L'ORÉAL SA L'ORÉAL USA Products Inc. (Official agent for L'ORÉAL SA) 30 Terminal Ave Clark, NJ 07066	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER N021502
2. TELEPHONE NUMBER (Include Area Code) (732) 680-5562	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: <u>PRE-SUBMISSION</u> Note: Partial payments previously made (APPLICATION NO. CONTAINING THE DATA).
3. PRODUCT NAME Mexoryl® SX 15 (ecamsule)	6. USER FEE I.D. NUMBER 4690

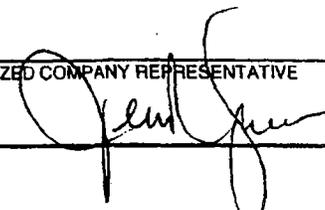
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 and 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Assistant Vice President Drug Approval Group	DATE 12-10-04
---	--	------------------

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

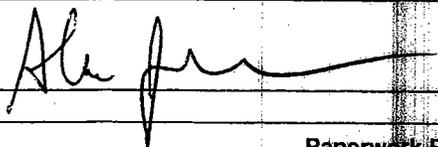
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)). See appended list
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME ALAN J. MEYERS	TITLE Senior Vice President, Research & Development
FIRM / ORGANIZATION L'ORÉAL USA Products, Inc. US Agent for L'ORÉAL SA	
SIGNATURE 	DATE 4/25/05

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

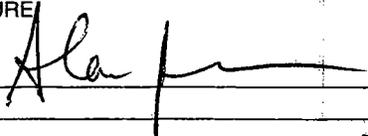
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)). See appended list
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME ALAN J. MEYERS	TITLE Senior Vice President, Research & Development
FIRM / ORGANIZATION L'ORÉAL USA Products, Inc. US Agent for L'ORÉAL SA	
SIGNATURE 	DATE 4/25/05

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Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

Department Of Health and Human Services
Food and Drugs Administration
Center for Drug Evaluation and Research
Office of New Drugs
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266
(301) 796-2060

Date: 7-21-06

From: Charles J. Ganley, M.D. _____
Director, Office of Nonprescription Products (HFD-560)
Office of New Drugs
Center for Drug Evaluation and Research

Subject: NDA 21-502 / Anthelios Sx

NDA 21-502 is a sunscreen product that includes three sunscreen ingredients. Originally, the sponsor (Loreal) submitted numerous labels with different trade names and package configurations. Within the past week, the [redacted] requested some changes in the proposed label because of some concerns about implied claim: [redacted]. The sponsor decided to withdraw the labeling for many of the products except for one with the trade name Anthelios Sx.

Anthelios Sx is configured as a 3.4 oz bottle with labeling that suggests this product is to be marketed primarily as a moisturizer with a sunscreen. It is likely this product is to be directed at women who would apply it to their face or hands in the morning. There are several cosmetic statements on the principle display panel that could be misleading if it were to be used as "sunscreen". The statements include: 1) Daily Moisturizing Cream; 2) Daily Use Moisturizer; 3) 24 hr long lasting moisturizer. These statements could be misleading for a sunscreen product because they suggest that the product will last the entire day. If used primarily as a sunscreen, these statements could lead someone to believe the sunscreen will provide protection throughout the day without reapplication (Drug Facts directions state to reapply as needed). This could be a problem if the sponsor increases the package size amount.

In order to make it clear that the approval applies to this specific product, the approval letter should include a statement that instructs the sponsor to submit a prior approval supplement if the package size is increased. If they want to increase the package amount, there may need to be clarifying language on the principle display panel that makes it clear that reapplication may be necessary for sun protection.

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/s/

Charles Ganley
7/21/2006 03:38:48 PM
MEDICAL OFFICER



**OTC Drug Labeling Review Addendum
for L'Oreal SPF 15 Sunscreens
(NDA [] 21-502)**

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATE: July 20, 2006

RECEIVED DATE: July 21, 2006

REVIEW DATE:

July 21, 2006

NDA/SUBMISSION TYPE:

NDA's . ——— 21-502 (N-000)

SPONSOR/CONTACT:

Jean R. Grieve
Assistant Vice President – Drug Approval
Group
Research & Development Division
L'Oreal USA Products, Inc.
111 L'Oreal Way
Clark, NJ 07066
732-680-5562
732-396-7051 (FAX)

DRUG PRODUCT:

—————
NDA 21-502: SPF15 Sunscreen Lotion

ACTIVE INGREDIENTS:

[]
NDA 21-502:
Avobenzone, 2%
Ecamsule, 2%
Octocrylene, 10%

INDICATIONS:

Prevention of sunburn ——— due to
sun exposure by providing broad spectrum
protection from UVB and UVA radiation

PHARMACOLOGICAL CATEGORY:

Sunscreen (broad spectrum)

LABELING SUBMITTED:NDA 21-502LaRoche-Posay ANTHELIOS SX¹¹ 100 ml tube**REVIEWER:**

Michael L. Koenig, Ph.D.

TEAM LEADER:

Matthew Holman, Ph.D.

BACKGROUND

As part of NDA [redacted] 21-502, the sponsor submitted labeling for [redacted] sunscreens to be marketed under a total of [redacted] trade names [redacted] NDA 21-502). On March 11, 2006, FDA sent an approvable (AE) letter to the sponsor based primarily on labeling deficiencies. Following submission of revised labeling from the sponsor, FDA communicated labeling deficiencies on the following dates:

- June 13, 2006
- July 18, 2006

Subsequently, the sponsor submitted revised labeling for the LaRoche-Posay product under NDA 21-502. In the same submission, the sponsor indicates that it is withdrawing all other labeling under NDA 20-502. [redacted]

2 Page(s) Withheld

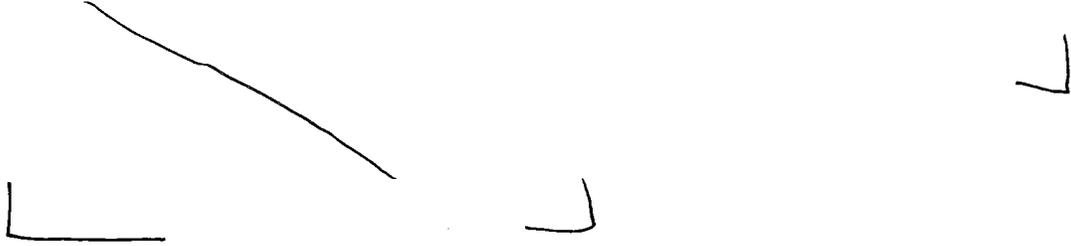
_____ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

✓ _____ § 552(b)(5) Deliberative Process

RECOMMENDATIONS

1.



2. Send the sponsor an approval (AP) letter for LaRoche-Posay Anthelios SX under NDA 21-502. Inform the sponsor that it must make the following revisions to the labeling submitted on July 21, 2006:

- a. Replace — with “wavelengths” in every occurrence on the labels.
- b. Remove — from the third bulleted statement under *Uses* so that it reads, “helps provide protection from UVA rays (short and long wavelengths).”

Remind the sponsor that it must submit a prior approval supplement if it wishes to market the following products under NDA 21-502:



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/s/

Matthew Holman
7/21/2006 03:43:50 PM
INTERDISCIPLINARY



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation

FACSIMILE TRANSMITTAL SHEET

DATE: June 22, 2006

To: Jean Grieve	From: Elaine Abraham Project Manager
Company: L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
Fax number: (732) 909-2007	Fax number: (301) 796-9899
Phone number: (732) 680-5562	Phone number: (301) 796-0843
Subject: NDA — 21-502 information request	

Total no. of pages including cover: 2

Comments:

Document to be mailed:	YES	NO
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We reference your NDA _____ 21-502 and have the following request for information:

We are aware that you have submitted an amendment to NDA _____

_____. Since the conversion factor - was also proposed in your 4/12/06 amendments of NDA _____ 21-502, please submit amendments to NDA _____ 21-502 to eliminate the use of the conversion factor.

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/s/

Elaine Abraham
6/22/2006 07:50:31 AM
CSO

NDA 21-502

Page 2

satisfaction of the requirements in section 2 of PREA alone may not qualify you for pediatric exclusivity.

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

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl
6/16/2006 10:17:40 AM

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_____ § 552(b)(4) Draft Labeling

✓ _____ § 552(b)(5) Deliberative Process

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

_____ § 552(b)(4) Draft Labeling

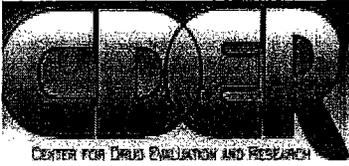
✓ § 552(b)(5) Deliberative Process

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process



**OTC Drug Labeling Review Addendum
for L'Oreal Sunscreens (NDA []
21-502)**

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATES:

[]

May 12, 2005 and
May 18, 2006
(NDA 21-502)

RECEIVED DATES:

[]

May 12, 2005 and
May 22, 2006
(NDA 21-502)

REVIEW DATE:

June 6, 2006

NDA/SUBMISSION TYPE:

NDA [] 21-502 (N-000/BL)

SPONSOR/CONTACT:

Jean R. Grieve
Assistant Vice President – Drug Approval
Group
Research & Development Division
L'Oreal USA Products, Inc.
111 L'Oreal Way
Clark, NJ 07066
732-680-5562
732-909-2007 (FAX)

DRUG PRODUCT:

[]
NDA 21-502: Moisturizer with SPF15
Sunscreen Cream

ACTIVE INGREDIENTS:

[]

NDA 21-502:
Avobenzone, 2%
Ecamsule, 2%
Octocrylene, 10%

INDICATIONS:

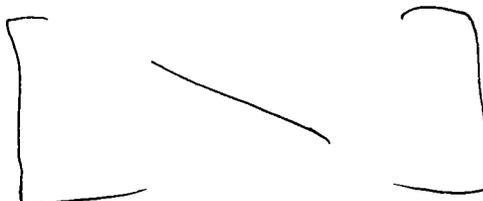
Prevention of sunburn due to sun exposure by providing broad spectrum protection from UVB and UVA radiation

PHARMACOLOGICAL CATEGORY:

Sunscreen (broad spectrum)

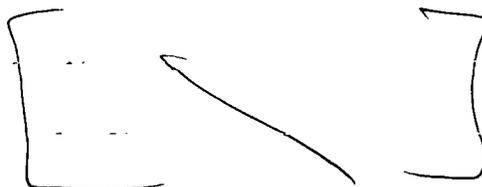
LABELING SUBMITTED:

Carton & immediate container labels for the following products:



NDA 21-502

- LaRoche-Posay ANTHELIOS SX



All products are 3.4 oz. (100 g) tubes unless noted above.

REVIEWER:

Michael L. Koenig, Ph.D.

TEAM LEADER:

Matthew Holman, Ph.D.

BACKGROUND

In response to a March 10, 2006, approvable letter recommending changes to the labeling for NDA 21-502, the sponsor submitted revised labeling on May 18, 2006. A total of 11 labels were resubmitted for the sunscreens (NDA 21-502). The sunscreens have identical trade names in

4 Page(s) Withheld

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 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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/s/

Michael Koenig
6/13/2006 08:58:16 AM
INTERDISCIPLINARY

Matthew Holman
6/13/2006 09:10:23 AM
INTERDISCIPLINARY

RECORD OF TELEPHONE CONVERSATION

Date: February 28, 2006
Project Manager: Elaine Abraham
Subject: Discuss labeling
NDA: — 21-502
Sponsor: L'Oreal
Product Name: SPF-15 Sunscreen
Phone No: (732) 680-5562

FDA participant: Elaine Abraham, RPM

L'Oreal participant: Jean Grieve, Assistant VP, R&D, Drug Approval Group

Discussion: FDA emailed labeling comments on NDA — 21-502 to L'Oreal on February 22, 2006. Since the due date for the applications is March 10, 2006, I called L'Oreal and told Ms. Grieve that we would need their draft labeling by March 6 in order to have time to review it prior to the due date. Ms. Grieve stated that because they have multiple trade names and — labels for their — NDAs and they also contract their labeling out, that it was unlikely they would submit revised labeling by March 6.

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/s/

Elaine Abraham
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CSO



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation

FACSIMILE TRANSMITTAL SHEET

DATE: February 22, 2006

To: Jean Grieve	From: Elaine Abraham Project Manager
Company: L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
Fax number: (732) 909-2007	Fax number: (301) 796-9899
Phone number: (732) 680-5562	Phone number: (301) 796-0843
Subject: NDA — 21-502 labeling comments	

Total no. of pages including cover: 4

Comments:

Document to be mailed: YES NO

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Please refer to your new drug applications NDA 20-502 — dated May 12 and 16, 2005 respectively for your OTC SPF 15 sunscreen products.

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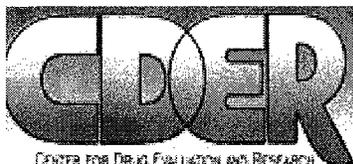
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/s/

Elaine Abraham
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OTC Drug Labeling Review for L'Oreal Sunscreens (NDA [] 21-502)

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration

SUBMISSION DATE: []
May 12, 2005
(NDA 21-502)

RECEIVED DATE: []
May 12, 2005
(NDA 21-502)

REVIEW DATE: February 21, 2006

NDA/SUBMISSION TYPE: NDA [] 21-502 (N-000)

SPONSOR/CONTACT: Jean R. Grieve
Assistant Vice President – Drug Approval Group
Research & Development Division
L'Oreal USA Products, Inc.
111 L'Oreal Way
Clark, NJ 07066
732-680-5562
732-396-7051 (FAX)

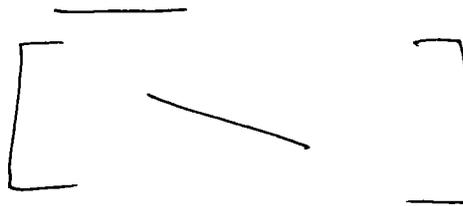
DRUG PRODUCT: []
NDA 21-502: SPF15 Sunscreen Lotion

ACTIVE INGREDIENTS: []
NDA 21-502:
Avobenzone, 2%
Ecamsule, 2%
Octocrylene, 10%

INDICATIONS: Prevention of sunburn _____ due to sun exposure by providing broad spectrum protection from UVB and UVA radiation

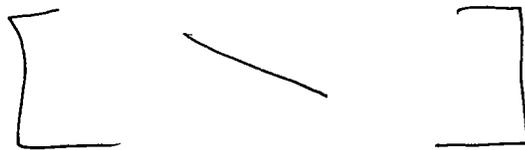
PHARMACOLOGICAL CATEGORY: Sunscreen (broad spectrum)

LABELING SUBMITTED:



NDA 21-502

LaRoche-Posav ANTHELIOS¹



' 100 ml tube

REVIEWER:

Michael L. Koenig, Ph.D.

TEAM LEADER:

Matthew Holman, Ph.D.

BACKGROUND

As part of NDA. ——— 21-502, the sponsor submitted labeling for — sunscreens to be marketed under a total of — trade names ([———] NDA 21-502). The — sunscreens have identical trade names in — cases: [———]

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/s/

Michael Koenig
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INTERDISCIPLINARY

Matthew Holman
2/21/2006 11:18:32 AM
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MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: January 31, 2006

FROM: Susan McCune, MD
Division of Pediatric Drug Development, OCTAP

Dianne L. Kennedy, MPH, RPH
Pregnancy & Lactation Team, OND

THROUGH: Sandra Kweder, MD
Deputy Director, OND

TO: Elaine Abraham, RPM
DNCE

SUBJECT: Combination OTC Sunscreens (Investigational Name - _____
and Use During Pregnancy
NDAs: _____ 21-502, _____ (L'Oreal USA Products)

Consult received by the PLT: December 8, 2005
Due date: January 31, 2006

I. EXECUTIVE SUMMARY

L'Oreal USA Products is seeking approval to market _____ new sunscreen products with three _____ sunscreen ingredients in differing concentrations. These ingredients are avobenzone, octocrylene, _____ (all _____ monograph ingredients) and ecamsule (a new ingredient). Eleven women became pregnant during three studies, four infants developed birthmarks: two with hemangiomas, one with a nevus flammeus and one with a café au lait spot.

The Pregnancy & Lactation Team (PLT) was consulted to

1. Provide feedback on whether or not the sponsor should conduct studies to evaluate children of mothers exposed to the new sunscreen formulations during pregnancy for cutaneous vascular abnormalities.
2. Advise whether the OTC labeling for these new sunscreen products should carry any pregnancy warnings.

The PLT recommends that the sponsor be requested to provide more descriptive information on the seriousness and extent of vascular involvement for the two

cases of hemangiomas as well as the dose and duration of exposure to the drug. Given that hemangiomas develop postnatally frequently (7 – 10% of infants) and most are small and involute, the PLT does not recommend setting up a pregnancy exposure registry unless there is something unusual about the two cases, e.g., very large, life-threatening, deep, etc.

The PLT does not recommend requiring a pregnancy warning on the OTC labeling for these products for the following reasons:

- Ecamsule is a Pregnancy Category B drug according to the Pharm/Tox review.
- PK studies show that <1% of ecamsule is absorbed systemically
- There is no evidence of reproductive toxicity for _____ ecamsule, avobenzone or octocrylene in the literature although the data are sparse.
- There are no reports in the literature or in AERS of hemangiomas associated with the use of _____ ecamsule, avobenzone or octocrylene.

II. BACKGROUND

The following was information provided in the written consult request:

“The sponsor is requesting approval to market _____ new sunscreen drug products _____ in the over-the-counter setting (NDA _____, 21-502, _____). All _____ sunscreens contain three _____ active sunscreen ingredients in _____ _____ avobenzone, octocrylene, _____ (all _____ monograph ingredients) and ecamsule (a new ingredient). [_____]

Altogether, 11 women became pregnant during studies with _____ formulas or similar formulations. One woman (Subject #60 in Study _____) discontinued due to pregnancy and withdrew from treatment and the study. The remaining 10 women became pregnant during 2 or 4 long-term safety studies _____ 750.02 and _____). There were no pregnancies reported during any other studies.

Four women became pregnant in Study _____ 750.02. Two of these subjects (#12-18 and #16-35) delivered during the study. Subject 11-16 discontinued the study prior to giving birth and subject 12-36 gave birth after completing the study. All four women delivered normal healthy babies.

Six pregnancies were reported during Study _____. Of the six women who reported pregnancy, three discontinued because of their pregnancy. Two of the six pregnancies resulted in a delivery of normal healthy babies. One infant developed a café au lait spot 1 to 2 weeks after birth. Since isolated café au lait spots occur in up to 10-20% of the normal population, the event was assessed

by the sponsor as of no pathological significance. Three of six infants were normal at birth but subsequently developed vascular lesions approximately three months after birth. All three events of birthmarks (two hemangiomas and one nevus flammeus) were reported as serious adverse events (congenital anomaly). Family history was negative in two cases and positive in one (nevus flammeus). For the two cases of hemangioma, the events were considered possibly related to study treatment; the case of nevus flammeus was considered of unlikely relationship to study treatment.

According to the pharmacology review, ecamsule is a Pregnancy Category B drug. Based on the preclinical data, ecamsule is not a teratogen and does not have an effect on reproductive function in animals. The division does not have data for the other two monograph active ingredients (avobenzone and octocrylene), which are not contraindicated in pregnancy. The number of women exposed to the sunscreen formulations containing ecamsule is small. Three congenital vascular adverse events occurred in subjects with _____ could have occurred by chance alone. Nevertheless, the exposure to drug product could be significant if used as directed. PK studies show that <1% of ecamsule (active ingredient) is absorbed systemically.”

III. REVIEW OF DATA

The following materials were reviewed:

- Medical Officer review of NDA _____
- Pharm/Tox review of NDA _____
- Reprotox information in the online Micromedex Intergrated Index including Teris – The Teratogen Information System, the Reprotox System and Shepard’s Catalog of Teratogenic Agents
- AERs database
- Pubmed for 1. reproductive effects with avobenzone, octocrylene, _____ or ecamsule and 2. hemangiomas. The following articles were retrieved.
 - Blei F. Basic science and clinical aspects of vascular anomalies. *Current Opinion in Pediatrics* 2005;17:5011-9.
 - Chiller KG, Frieden IJ, Arbiser JL. Molecular pathogenesis of vascular anomalies: Classification into three categories based upon clinical and biochemical characteristics. *Lymphatic Research and Biology* 2003;1(4):267-81.
 - Chang MW. Updated classification of hemangiomas and other vascular anomalies. *Lymphatic Research and Biology* 2003;1(4):259-65.

The medical officer review and the pharm/tox review are from the previous submission (____). There is no information from the current submission other than what is included in the written consult. It appears that 3 studies contained women who became pregnant (N=11). One woman in study _____ became pregnant and

discontinued her participation in the trial. Four women in study — 750.02 became pregnant and all delivered healthy babies. Six pregnancies were reported in study _____ which was reviewed for NDA — Of the 6 pregnancies, 3 infants developed "vascular lesions" approximately 3 months after birth. One was a nevus flammeus and two were reported as hemangiomas. There was no description of the hemangiomas. Dr. Eichenfield at UCSD stated that nevus flammeus is present in half of all newborns and hemangiomas occur in 10-13% of children in the first year of life. He was unaware of any reports that hemangiomas have been induced by exogenous factors such as drugs or chemicals. He felt that the hemangiomas were random findings and not related to the use of the sunscreen.

The consult mentions another patient with a cafe au lait spot but that is not discussed in the medical officer review of NDA — According to the consult, the cafe au lait spot was felt to be of no pathological significance "since isolated cafe au lait spots occur in up to 10-20% of the normal population".

In the Pharm/Tox review of NDA — there was an oncogenicity study by dermal application of ecamsule to CD-1 mice for 104 weeks (p.45-51). They concluded, "The relative incidence of hemangiosarcomas compared to controls was higher in the high dose males and females. The relative incidence of hemangiomas in treated females was also increased over control. However, hemangiomas and hemangiosarcomas are not rare in the historical control data from the testing laboratory and the values from the current study appear to be within historical control ranges."

There is no evidence of reproductive toxicology for _____ ecamsule, avobenzone or octocrylene in the literature although the data are sparse.

There are no reports in the literature of hemangiomas associated with ecamsule, avobenzone, octocrylene, _____

In a search of the AERS database for ecamsule, avobenzone, octocrylene, _____ and _____ there were a total of 61 reports. None of them mentioned hemangioma. There were no AERS reports for any children between 0-1 year of age, and there were no reports of congenital anomalies.

The literature supports the assessment that nevus flammeus occurs in approximately half of all newborns, cafe au lait spots in approximately 10 % of infants and hemangiomas in approximately 7-10% of the newborn population. Hemangiomas are more common in female infants and premature infants. They tend to grow postnatally for several months and then spontaneously involute. There are many varieties of hemangiomas in the newborn period and there was no description of the type of hemangioma in the study report. The etiology of vascular anomalies in the newborn period is unclear and likely represents a multifactorial process.

IV. CONCLUSIONS

Cutaneous vascular abnormalities occur frequently in the newborns. Unless the two cases of hemangiomas reported in the study are unusual for some reason, e.g., very large, life-threatening, deep, etc. the PLT does not see a need for a pregnancy exposure registry.

Based on the materials reviewed the PLT does not recommend a pregnancy warning be included in the OTC labeling.

Susan McCune, MD
Division of Pediatric Drug Development,
OCTAP

Dianne L. Kennedy, MPH, RPh
Pregnancy & Lactation Team,
OND

Cc: OND: Kweder, Kennedy
DPPD: Mathis, McCune
DNCE: Leonard Segal, Abraham

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/s/

Matthew Bacho

2/1/2006 01:55:32 PM

CSO

PLT Consult for NDA: _____ 21-502

Sandra L. Kweder

2/8/2006 05:42:15 PM

MEDICAL OFFICER

4 Page(s) Withheld

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

§ 552(b)(4) Draft Labeling

§ 552(b)(5) Deliberative Process

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Division of Medication Errors and Technical Support (DMETS) WO22 Bldg., Rm. 4412		FROM: Elaine Abraham, RPM Div. of Nonprescription Clinical Evaluation, WO22, Rm. 5410		
DATE January 5, 2006	IND NO.	NDA NO. — 21-502	TYPE OF DOCUMENT	DATE OF DOCUMENT May 12, 2005
NAME OF DRUG Anthelios SPF 15 Sunscreens (ecamsule/avobenzone/octocrylene)	PRIORITY CONSIDERATION High	CLASSIFICATION OF DRUG I,4S Sunscreen	DESIRED COMPLETION DATE January 31, 2006	
NAME OF FIRM: L'Oreal USA Products				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review only				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: We are requesting a trade name review of the name "Anthelios". (This is one of numerous trade names for sunscreen NDAs that we are sending you.) We are not interested in a Drug Facts review, as all Drug Facts labeling is identical for these NDAs, and you have already provided your comments on this. The PDUFA date for these NDAs is March 12, 2006. A paper copy of this consult and labeling will follow in inter-office mail. Please contact me at 796-0843 if you have any questions.				
SIGNATURE OF REQUESTER †See appended electronic signature page†		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Elaine Abraham
1/5/2006 01:54:48 PM

12 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): PLT Consult Coordinator Pregnancy and Lactation Team		FROM: Elaine Abraham, RPM Office of Nonprescription Products		
DATE December 8, 2005	IND NO.	NDA NO. NDA: _____ 21-502, _____	TYPE OF DOCUMENT New NDAs	DATE OF DOCUMENT
NAME OF DRUG Combination sunscreen (Investigational name- _____)	PRIORITY CONSIDERATION High	CLASSIFICATION OF DRUG Sunscreen	DESIRED COMPLETION DATE January 31, 2006	
NAME OF FIRM: L'Oreal USA Products				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL	<input type="checkbox"/> PRE--NDA MEETING	<input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER		
<input type="checkbox"/> PROGRESS REPORT	<input type="checkbox"/> END OF PHASE II MEETING	<input type="checkbox"/> FINAL PRINTED LABELING		
<input type="checkbox"/> NEW CORRESPONDENCE	<input type="checkbox"/> RESUBMISSION	<input checked="" type="checkbox"/> LABELING REVISION		
<input type="checkbox"/> DRUG ADVERTISING	<input checked="" type="checkbox"/> SAFETY/EFFICACY	<input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE		
<input type="checkbox"/> ADVERSE REACTION REPORT	<input type="checkbox"/> PAPER NDA	<input type="checkbox"/> FORMULATIVE REVIEW		
<input type="checkbox"/> MANUFACTURING CHANGE/ADDITION	<input type="checkbox"/> CONTROL SUPPLEMENT	<input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):		
<input type="checkbox"/> MEETING PLANNED BY				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW		<input type="checkbox"/> CHEMISTRY REVIEW		
<input type="checkbox"/> END OF PHASE II MEETING		<input type="checkbox"/> PHARMACOLOGY		
<input type="checkbox"/> CONTROLLED STUDIES		<input type="checkbox"/> BIOPHARMACEUTICS		
<input type="checkbox"/> PROTOCOL REVIEW		<input type="checkbox"/> OTHER (SPECIFY BELOW):		
<input type="checkbox"/> OTHER (SPECIFY BELOW):				
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE		
<input type="checkbox"/> BIOAVAILABILITY STUDIES		<input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS		
<input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY		
<input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES		<input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE		
<input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below)		<input type="checkbox"/> POISON RISK ANALYSIS		
<input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP				
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		

COMMENTS/SPECIAL INSTRUCTIONS:

Please provide your feedback on whether or not the sponsor should conduct studies to evaluate children of mothers exposed to the new sunscreen formulations during pregnancy for cutaneous vascular abnormalities. Also advise whether the OTC labeling for these new sunscreen drug products should carry any pregnancy warnings. Under current regulations, only OTC products intended for systemic use require to carry a pregnancy warning as specified in the 21 CFR 201.63 (a): "If pregnant or breast-feeding, ask a healthcare professional before use."

The sponsor is requesting an approval to market new sunscreen drug products in over-the-counter setting (NDA. 21-502, All sunscreens contain three active sunscreen ingredients in different concentrations: avobenzone, octocrylene, (all three monograph ingredients) and the new ingredient ecamsule.

Altogether, 11 women became pregnant during studies with formulas or similar formulations. One woman (Subject #60) in Study discontinued due to pregnancy and withdrew from treatment and the study. The remaining 10 women became pregnant during 2 of 4 long-term safety studies (750.02). There were no pregnancies reported during any other studies.

Four women became pregnant in Study 750.02. Two of these subjects (#12-18 and #16-35) delivered during the study. Subject 11-16 discontinued the study prior to giving birth and Subject 12-36 gave birth after completing the study. All four women delivered normal healthy babies.

Six pregnancies were reported during Study . Of the six women who reported pregnancy, three discontinued because of their pregnancy. Two of the six pregnancies resulted in a delivery of normal healthy babies. One infant developed a café au lait spot 1 to 2 weeks after birth. Since isolated café au lait spots occur in up to 10-20% of the normal population, the event was assessed by the sponsor as of no pathological significance. Three of six infants were normal at birth but subsequently developed vascular lesions approximately three months after birth. All three events of birthmarks (two hemangiomas and one nevus flammeus) were reported as serious adverse events (congenital anomaly). Family history was negative in two cases and positive in one (nevus flammeus). For the two cases of hemangioma, the events were considered possibly related to study treatment; the case of nevus flammeus was considered of unlikely relationship to study treatment.

According to the pharmacology review, ecamsule is a Pregnancy Category B drug. Based on the preclinical data, ecamsule is not a teratogen and does not have an effect on reproductive function in animals. We do not have data for the other two monograph active ingredients (avobenzone and octocrylene), which are not contraindicated during pregnancy. The number of women exposed to the sunscreen formulations containing ecamsule is small. Three congenital vascular adverse events occurred in subjects with could have occurred by chance alone. Nevertheless, the exposure to drug product could be significant if used as directed. PK studies show that <1% of ecamsule (active ingredient) is absorbed systemically.

SIGNATURE OF REQUESTER Elaine Abraham, RPM, (301) 796-0843	METHOD OF DELIVERY (Check one) MAIL <input type="checkbox"/> HAND <input type="checkbox"/>
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Elaine Abraham
12/8/2005 01:02:24 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Office/Division): Lisa Mathis, Division Director Division of Pediatric Drug Development		FROM (Name, Office/Division, and Phone Number of Requestor): Elaine Abraham, RPM Division of Nonprescription Clinical Evaluation		
DATE December 8, 2005	IND NO.	NDA NO. — 21-502	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT
NAME OF DRUG ecamsule, avobenzone, octocrylene SPF 15 sunscreen		PRIORITY CONSIDERATION High	CLASSIFICATION OF DRUG 14S	DESIRED COMPLETION DATE January 31, 2006
NAME OF FIRM: L'Oreal USA Products				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> END-OF-PHASE 2a MEETING <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> END-OF-PHASE 2 MEETING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> SAFETY / EFFICACY <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION <input type="checkbox"/> PAPER NDA <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> CONTROL SUPPLEMENT				
II. BIOMETRICS				
<input type="checkbox"/> PRIORITY P NDA REVIEW <input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> END-OF-PHASE 2 MEETING <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW): <input type="checkbox"/> OTHER (SPECIFY BELOW):				
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS <input type="checkbox"/> PHASE 4 STUDIES <input type="checkbox"/> IN-VIVO WAIVER REQUEST				
IV. DRUG SAFETY				
<input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> POISON RISK ANALYSIS <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP				
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL <input type="checkbox"/> NONCLINICAL				
COMMENTS / SPECIAL INSTRUCTIONS: See attached.				
SIGNATURE OF REQUESTOR Elaine Abraham, RPM, (301) 796-0843			METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND	
PRINTED NAME AND SIGNATURE OF RECEIVER			PRINTED NAME AND SIGNATURE OF DELIVERER	

NDA ——— ' 21-502 Peds consult attachment

Please provide a written memo to the file on whether pediatric studies should be requested for children under 6 months of age for a sunscreen product. Include the rationale for your decision. The sponsor is requesting to market ——— the combination sunscreen products in the OTC setting for daily use in children six months of age and older and in adults.

During the end-of-phase 2 meeting, FDA requested the sponsor to include children six months or older into the study — 750.02, and recommended that at least 50% of the subjects be below 12 years. In addition, FDA recommended including children ages 6 months to 12 years in both studies — 750.01 and ——— (population). As an alternative to the pediatric — patients, FDA recommended studying at least 100 pediatric subjects > 6 months to 12 years of age in a separate long-term study of ——— cream. Only 64 children were included in the safety population in — 750.03. However, 179 children 6 months to 12 years of age (73% of all subjects) were enrolled and 69% of them (124/179) completed — 750.02.

A total of 243 children 6 months to 12 years old participated in the ——— long term use clinical trials. There were no children under 12 years old included in the daily use study — 750.01. Of 79 subjects in intermittent use study — 750.03, 64 children 6 months to 12 years of age (81% of all subjects, 55 pediatrics completed the study) were included in the safety population. Additionally, in intermittent use study — 750.02, 179 children 6 months to 12 years of age (73% of all subjects) were enrolled and 69% (124/179) of these children completed. While — 750.02 was conducted on a different — formula ——— than the ——— formulations, it contained a higher concentration of the new chemical entity, ecamsule, than did 539-009 used for — 750.03.

In addition, ecamsule is being marketed for children in Europe since 1996.

The question is whether we need safety or efficacy data for these new sunscreen products in children below 6 months of age. Clinical practice guidelines published by the American Academy of Pediatrics (AAP) do not recommend using sunscreens in children less than 6 months of age for the following reasons:

1. Since children of this age are not mobile and cannot remove themselves from uncomfortable light and heat, they should be kept out of direct sunlight, in shade.
2. Many infants have impaired functional sweating. Exposure to the heat of the sun may increase the risk of heatstroke.
3. Sunburn may occur readily because an infant's skin has less melanin than at any other time in life.
4. Concerns are raised that human skin under 6 months may have different absorptive characteristics; biologic systems that metabolize and excrete drugs may not be fully developed.

AAP further states that, it may be reasonable to apply sunscreen to small areas, such as the face and the back of the hands when the infant's skin is not protected adequately by clothing.

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/s/

Elaine Abraham
12/8/2005 12:23:35 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): David Hussong, Director Department of Microbiology, HFD-805 White Oak Building #21, Room 3654 10903 New Hampshire Avenue Silver Spring, MD 20993		FROM: Sue-Ching Lin, Review Chemist Branch V, Office of New Drug Quality Assessment White Oak Building #22, Room 2443 10903 New Hampshire Avenue Silver Spring, MD 20993		
DATE November 18, 2005	IND NO.	NDA NO. 21-502,	TYPE OF DOCUMENT Original NDAs	DATE OF DOCUMENT 5/12/05
NAME OF DRUG		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG sunscreens	DESIRED COMPLETION DATE ASAP
NAME OF FIRM: L'Oreal USA Products, Inc.				
REASON FOR REQUEST				
I. GENERAL				
NEW PROTOCOL PROGRESS REPORT NEW CORRESPONDENCE DRUG ADVERTISING ADVERSE REACTION REPORT MANUFACTURING CHANGE/ADDITION MEETING PLANNED BY		PRE-NDA MEETING END OF PHASE II MEETING RESUBMISSION SAFETY/EFFICACY PAPER NDA CONTROL SUPPLEMENT	RESPONSE TO DEFICIENCY LETTER FINAL PRINTED LABELING LABELING REVISION ORIGINAL NEW CORRESPONDENCE FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):	
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH	
TYPE A OR B NDA REVIEW END OF PHASE II MEETING CONTROLLED STUDIES PROTOCOL REVIEW OTHER (SPECIFY BELOW):			CHEMISTRY REVIEW PHARMACOLOGY BIOPHARMACEUTICS OTHER (SPECIFY BELOW):	
III. BIOPHARMACEUTICS				
DISSOLUTION BIOAVAILABILITY STUDIES PHASE IV STUDIES			DEFICIENCY LETTER RESPONSE PROTOCOL-BIOPHARMACEUTICS IN-VIVO WAIVER REQUEST	
IV. DRUG EXPERIENCE				
PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES CASE REPORTS OF SPECIFIC REACTIONS (List below) COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY SUMMARY OF ADVERSE EXPERIENCE POISON RISK ANALYSIS	
V. SCIENTIFIC INVESTIGATIONS				
CLINICAL			PRECLINICAL	
COMMENTS/SPECIAL INSTRUCTIONS: Please review the NDAs with regard to microbiological aspects, including antimicrobial effectiveness test results, and the drug product specification (acceptance criteria for the microbial limits test, preservatives, and the absence of the antimicrobial effectiveness test based on the previous test results). I have discussed the issues with Dr. Stephen Langille and he agreed to review the data.				
SIGNATURE OF REQUESTER Sue-Ching Lin, Review Chemist, ONDQA			METHOD OF DELIVERY (Check one) MAIL <input type="checkbox"/> HAND <input checked="" type="checkbox"/>	
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER	

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/s/

Moo-Jhong Rhee
11/21/2005 09:36:58 AM
Chief, Branch III



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation

FACSIMILE TRANSMITTAL SHEET

DATE: November 4, 2005

To: Jean Grieve	From: Elaine Abraham Project Manager
Company: L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
Fax number: (732) 909-2007	Fax number: (301) 796-9899
Phone number: (732) 680-5562	Phone number: (301) 796-0843
Subject: NDA — 21-502, — information request	

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2060. Thank you.

We reference your original NDA: — 21-502, — and have the following request for information:

The acceptance criteria for related substances in Table 4.A. 3-12 (drug product specification) appeared to exceed the ICH Q3B qualification thresholds. The safety of these related substances in the drug product should be addressed. This may be addressed with information demonstrating that these related substances were tested in clinical studies, nonclinical data, or data from human exposure to these related substances from other products.

Please provide:

- (1) the toxicology data available for these related substances and/or similar compounds
- (2) information on the levels of these impurities on the batches tested in clinical studies, and/or
- (3) information regarding these related substances in any marketed products including the specifications and human use data.

If any batch of the drug product which contained these related substances has been tested in the Pharmacology/Toxicology studies shown in Item 5, Table 5.1, please provide the results of batch data analysis or Certificates of Analysis, including the amounts of these related substances.

The acceptance criterion for “individual unknown” should be below the ICH Q3B qualification threshold (— for maximum daily dose of >2g).

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/s/

Elaine Abraham
11/4/2005 02:31:54 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

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 May 12, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 2% ecamsule/2% avobenzone /10% octocrylene lotion.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on July 11, 2005, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issue:

It is unclear which of the submitted studies were conducted using the to-be-marketed formulation of the proposed drug product.

We are providing the above comment to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We request that you submit the following information:

Provide a list of all the studies submitted to NDA 21-502 that were conducted using the to-be-marketed formulation of the proposed drug product.

Please respond to the above request for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 827-2276.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Leah Christl
7/21/05 12:12:55 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Division of Medication Errors and Technical Support (DMETS), HFD-420 PKLN Bldg., Room 6-34		FROM: Elaine Abraham, RPM Div. of Nonprescription Clinical Evaluation, HFD-560		
DATE July 12, 2005	IND NO.	NDA NO. 21-502	TYPE OF DOCUMENT	DATE OF DOCUMENT May 12, 2005
NAME OF DRUG SPF 15 Daily Use Sunscreen (ecamsule/avobenzone/octocrylene)	PRIORITY CONSIDERATION High	CLASSIFICATION OF DRUG 1,4S Sunscreen	DESIRED COMPLETION DATE November 10, 2005	
NAME OF FIRM: L'Oreal USA Products				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		CHEMISTRY REVIEW PHARMACOLOGY BIOPHARMACEUTICS OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: We are requesting a trade name review for NDA 21-502. (We will also be sending a trade name consult for a related NDA <u> </u>) The PDUFA date for this NDA is March 12, 2006. The paper copy of consult and labeling to follow in inter-office mail. Please contact me at 827-2276 if you have any questions.				
Attachments: Sunscreen labels - <u> </u> LaRoche Posay Anthelios, <u> </u> <u> </u>				
SIGNATURE OF REQUESTER {See appended electronic signature page}		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Elaine Abraham
7/12/05 11:32:30 AM



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:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: 2% ecamsule/2% avobenzone /10% octocrylene lotion

Review Priority Classification: Standard (S)

Date of Application: May 12, 2005

Date of Receipt: May 12, 2005

Our Reference Number: NDA 21-502

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on July 11, 2005, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be March 12, 2006.

Under 21 CFR 314.102(c), you may request a meeting with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

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 note that you have submitted pediatric data with this application. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

NDA 21-502

Page 2

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Send all electronic or mixed electronic and paper submissions to the Central Document Room at the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

If your submission only contains paper, send it to one of the following address:

U.S. Postal Service:

Center for Drug Evaluation and Research
Office of Nonprescription Products, HFD-560
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products, HFD-560
Attention: Document Room
9201 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions, call Elaine Abraham, Regulatory Project Manager, at (301) 827-2276.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Chief, Project Management Staff
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
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/

Leah Christl

7/8/05 03:58:11 PM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-502 Supplement # Efficacy Supplement Type SE-

Trade Name: Various TNs - SPF 15 Daily Use Sunscreen
Established Name: Ecamsule 2%, Avobenzone USP 2%, Octocrylene USP 10%
Strengths:

Applicant: L'Oreal USA Products, Inc.
Agent for Applicant:

Date of Application: May 12, 2005
Date of Receipt: May 12, 2005
Date clock started after UN: N/A
Date of Filing Meeting: June 22, 2005
Filing Date: July 11, 2005
Action Goal Date (optional): February 12, 2006 User Fee Goal Date: March 12, 2006

Indication(s) requested: Prevention of sunburn and exposure to ultraviolet radiation (UVR)

Type of Original NDA: (b)(1) (b)(2)
OR
Type of Supplement: (b)(1) (b)(2)

NOTE:

- (3) *If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2), complete Appendix B.*
- (4) *If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:*

NDA is a (b)(1) application OR NDA is a (b)(2) application

Therapeutic Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 1,4
Other (orphan, OTC, etc.) OTC

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the*

Version: 12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.

product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO

If yes, explain:

- Does another drug have orphan drug exclusivity for the same indication? YES NO

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES NO

- Was form 356h included with an authorized signature? YES NO

If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO

If no, explain:

- If an electronic NDA, does it follow the Guidance? N/A YES NO

If an electronic NDA, all forms and certifications must be in paper and require a signature.

Which parts of the application were submitted in electronic format?

Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A YES NO

- Is it an electronic CTD (eCTD)? N/A YES NO

If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO

- Exclusivity requested? YES, 5 Years NO

NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- Correctly worded Debarment Certification included with authorized signature? YES NO

If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e.,
 “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as “To the best of my knowledge”

- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y NO
- PDUFA and Action Goal dates correct in COMIS? YES NO
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: 59,126 _____
- End-of-Phase 2 Meeting(s)? Date(s) 1/24/01 NO
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 9/18/01 NO
 If yes, distribute minutes before filing meeting.

Project Management

- Was electronic “Content of Labeling” submitted? YES NO
 If no, request in 74-day letter.
- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES NO
- Risk Management Plan consulted to ODS/IO? N/A YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to Florian Zielinski (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

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ATTACHMENT

MEMO OF FILING MEETING

DATE: 6/22/05

BACKGROUND: This NDA proposes a combination product containing ecamsule 2%, avobenzone USP 2%, octocrylene USP 10% for the prevention of sunburn following exposure to ultraviolet radiation (UVR). Ecamsule is a new molecular entity not previously approved in the U.S. Ecamsule has been commercially available outside the U.S. since 1993 and widely used globally in cosmetic sunscreen products. Avobenzone and octocrylene are OTC monograph ingredients.

(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES: See below, plus Andrea Leonard Segal, Markham Luke, Mohamed Al Osh, John Smith, Paul Brown

ASSIGNED REVIEWERS (including those not present at filing meeting) :

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Daiva Shetty
Secondary Medical:	Phyllis Huene
Statistical:	Steve Thomson
Pharmacology:	Jiaqin Yao
Statistical Pharmacology:	
Chemistry:	Sue-Ching Lin
Environmental Assessment (if needed):	
Biopharmaceutical:	Abi Adebawale
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	Roy Blay
Regulatory Project Management:	Elaine Abraham
Other Consults:	
Labeling:	Mike Koenig

Per reviewers, are all parts in English or English translation? YES NO
If no, explain:

CLINICAL FILE REFUSE TO FILE

- Clinical site inspection needed? YES NO
- Advisory Committee Meeting needed? YES, date if known _____ NO

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A YES NO

CLINICAL MICROBIOLOGY N/A FILE REFUSE TO FILE

STATISTICS N/A FILE REFUSE TO FILE

BIOPHARMACEUTICS FILE REFUSE TO FILE

- Biopharm. inspection needed?

YES NO

PHARMACOLOGY N/A FILE REFUSE TO FILE

- GLP inspection needed?

YES NO

CHEMISTRY FILE REFUSE TO FILE

- Establishment(s) ready for inspection?
- Microbiology

YES NO

YES NO

ELECTRONIC SUBMISSION:

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

(Refer to 21 CFR 314.101(d) for filing requirements.)

The application is unsuitable for filing. Explain why:

The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.

No filing issues have been identified.

Filing issues to be communicated by Day 74. List (optional): Review issue: It is unclear which of the submitted studies were conducted using the to-be-marketed formulation of the proposed drug product.

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.

2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.

3. Convey document filing issues/no filing issues to applicant by Day 74.

Elaine Abraham
Regulatory Project Manager, HFD-560

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Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

- (3) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (4) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (5) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (6) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):
3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved? YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," skip to question 4. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of*

Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, YES NO
ORP?

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product? YES NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (b) Is the approved drug product cited as the listed drug? YES NO

6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution"). This application provides for a new combination of a new molecular entity (ecamsule) and 2 OTC monograph ingredients (avobenzone and octocrylene).
7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9)). YES NO
No RLD
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
No RLD
10. Are there certifications for each of the patents listed for the listed drug(s)? YES NO
No listed drugs
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s):

- 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

Patent number(s):

- 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)

Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].

- 21 CFR 314.50(i)(1)(ii): No relevant patents.

- 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):

- 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).

Patent number(s):

- Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?

YES NO

Application relied on agency's previous finding of GRASE for avobenzone up to — octocrylene up to 10%,  under the Tentative Final Monograph for Sunscreen Drug Products for OTC Human Use (21 CFR 352).

- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

YES NO

- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

N/A YES NO

- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv)).?
N/A YES NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).
YES NO

Not specifically. Applicant claims 5 yrs exclusivity based on the NME, ecamsule and refers to 314.108(b)(2).

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.
YES NO

- EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

IND# 59,126 NO

OR

A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

YES NO

3. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES NO

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Elaine Abraham
3/21/2006 09:57:35 AM
CSO

Division of Dermatologic and Dental Drug Products (HFD-540)
Pharmacology/Toxicology Checklist for NDA Filing Meeting

Date: 6-22-2005
Reviewer: Jiaqin Yao
NDA Number: 21-502
Drug Name: _____ SPF 15 daily use moisturizing lotion sunscreen
(avobenzone 2%, ecamsule 2%, octocrylene 10%)
CAS Number: 70356-09-1, 6197-30-4, and 92761-26-7
Drug Class: sunscreen
Indication: Prevention of sunburn ☺ ☹ due to _____ sun exposure
Route of Administration: Topical
Date CDER Received: 5/12/2005
User Fee Date: 12/7/2004
Date of Draft Review: 1-15-2006
Sponsor: L'ORÉAL SA

Fileability:

On initial overview of the NDA application:

- (1) Does the pharmacology/toxicology section of the NDA appear to be organized in a manner to allow a substantive review to be completed?
Yes

- (2) Is the pharmacology/toxicology section of the NDA indexed and paginated in a manner to enable a timely and substantive review?
Yes

- (3) Is the pharmacology/toxicology section of the NDA sufficiently legible to permit a substantive review to be completed?
Yes

- (4) Are all required (*) and requested IND studies completed and submitted in this NDA (carcinogenicity, mutagenicity, teratogenicity*, effects on fertility*, juvenile studies, acute studies*, chronic studies*, maximum tolerated dosage determination, dermal irritancy, ocular irritancy, photocarcinogenicity, animal pharmacokinetic studies, etc)?
Yes

- (5) If the formulation to be marketed is different from the formulation used in the toxicology studies, has the Sponsor made an appropriate effort to either repeat the studies using the to be marketed product or to explain why such repetition should not be required?
Yes. A similar formulation with a higher concentration and more active ingredients has been used in the toxicology studies.

(6) Are the proposed labeling sections relative to pharm/tox appropriate (including human dose multiples expressed in either mg/m² or comparative serum/plasma levels) and in accordance with 201.57?

No

(7) Has the Sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the Sponsor?

Yes

(8) On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the Sponsor submitted a rationale to justify the alternative route?

Yes

(9) Has the Sponsor submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?

Yes

(10) Has the Sponsor submitted the data from the nonclinical carcinogenicity studies, in the STUDIES electronic format, for the review by Biometrics?

It will be determined by the Biostat reviewer.

(11) From a pharmacology perspective, is this NDA fileable? If "no", please state below why it is not.

Yes

(12) If the NDA is fileable, are there any issues that need to be conveyed to Sponsor? If so, specify:

None

(13) Issues that should not be conveyed to the Sponsor:

None

Pharmacology Reviewer

Pharmacology Supervisor

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Jiaqin Yao
6/22/05 02:34:15 PM
PHARMACOLOGIST

Paul Brown
6/22/05 04:57:49 PM
PHARMACOLOGIST

34 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

5 Page(s) Withheld

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

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST		
NDA 21-502	Efficacy Supplement Type SE-	Supplement Number
Drug: Anthelios SX (2% ecamsule/2% avobenzone /10% octocrylene) cream		Applicant: L'Oreal USA Products, Inc.
RPM: Elaine Abraham		HFD-560 Phone # (301) 796-0843
<p>Application Type: () 505(b)(1) (X) 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p>(X) Confirmed and/or corrected</p>	<p>Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Avobenzone (sunscreen monograph) Octocrylene (sunscreen monograph)</p>	
❖ Application Classifications:		
• Review priority		(X) Standard () Priority
• Chem class (NDAs only)		1,4
• Other (e.g., orphan, OTC)		OTC
❖ User Fee Goal Dates		
		March 12, 2006
❖ Special programs (indicate all that apply)		
		(X) None Subpart H () 21 CFR 314.510 (accelerated approval) () 21 CFR 314.520 (restricted distribution) () Fast Track () Rolling Review () CMA Pilot 1 () CMA Pilot 2
❖ User Fee Information		
• User Fee		(X) Paid UF ID number 4690
• User Fee waiver		() Small business () Public health () Barrier-to-Innovation () Other (specify)
• User Fee exception		() Orphan designation () No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) () Other (specify)
❖ Application Integrity Policy (AIP)		

<ul style="list-style-type: none"> • Applicant is on the AIP 	() Yes (X) No
<ul style="list-style-type: none"> • This application is on the AIP 	() Yes (X) No
<ul style="list-style-type: none"> • Exception for review (Center Director's memo) 	
<ul style="list-style-type: none"> • OC clearance for approval 	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	(X) Verified
❖ Patent	
<ul style="list-style-type: none"> • Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. 	(X) Verified
<ul style="list-style-type: none"> • Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) () Verified <i>N/A-No patents in OB</i>
<ul style="list-style-type: none"> • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	21 CFR 314.50(i)(1) () (ii) () (iii)
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).</i> • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).</p> <p><i>If "Yes," skip to question (4) below. If "No," continue with question (2).</i></p> <p>(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?</p> <p><i>If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).</i></p> <p><i>If "No," continue with question (3).</i></p> <p>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</p>	(X) N/A (no paragraph IV certification) () Verified
	() Yes () No
	() Yes () No
	() Yes () No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? () Yes () No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? () Yes () No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> • Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	
<ul style="list-style-type: none"> • Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	() Yes, Application # _____ () No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	6/21/05, 2/24/06

❖ Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	() Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes () Not applicable
• Indicate what types (if any) of information dissemination are anticipated	() None (X) Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	5/12/05, 5/18/06, 6/23/06, 7/10/06, 7/12/06, 7/20/06
• Original applicant-proposed labeling	5/12/05
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	12/9/05, 2/13/06 (mtg), 2/14/06, 2/21/06, 3/8/06, 3/9/06 (2), 6/13/06, 7/13/06, 7/21/06
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	
• Reviews	
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	PREA commitment
• Documentation of discussions and/or agreements relating to post-marketing commitments	
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	7/21/05, 11/4/05, , 2/22/06, 6/13/06, 6/22/06
❖ Memoranda and Telecons	1/23/06, 2/14/06
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	1/24/01
• Pre-NDA meeting (indicate date)	9/18/01
• Pre-Approval Safety Conference (indicate date; approvals only)	
• Other	
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	5/21/99 (64 FR 27666)

❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	3/6/06, 7/10/06
❖ Clinical review(s) (indicate date for each review)	10/17/05, 1/6/06, 1/9/06, 2/15/06
❖ Microbiology (efficacy) review(s) (indicate date for each review)	
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	1/6/06 clin review, 2/15/06
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	7/14/06
❖ Demographic Worksheet (NME approvals only)	
❖ Statistical review(s) (indicate date for each review)	N/A
❖ Biopharmaceutical review(s) (indicate date for each review)	2/21/06
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	
• Bioequivalence studies	
CMC Information	
❖ CMC review(s) (indicate date for each review)	3/2/06, 7/7/06
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	
• Review & FONSI (indicate date of review)	
• Review & Environmental Impact Statement (indicate date of each review)	
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	11/30/05
❖ Facilities inspection (provide EER report)	Date completed: 3/16/06 (X) Acceptable () Withhold recommendation
❖ Methods validation	() Completed N/A () Requested () Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	2/2/06
❖ Nonclinical inspection review summary	
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	
❖ CAC/ECAC report	8/31/05

Appendix A to NDA/Efficacy Supplement Action Package Checklist

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).