CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 21-501

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

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

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
21-501

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)
VARIOUS CAPITAL SOLEIL Sunscreen; UV EXPERT Sunscreen; ANTHELIOS Sunscreen;

ACTIVE INGREDIENT(S)	STRENGTH(S)
ecamsule	3%
avobenzone	2%
octocrylene	10%

RECEIVED
OCT 07 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)*
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)

Norman H. Stepno, Esquire
Burns, 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

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.

7,309,511

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?	☒ 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.**

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	☒ 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)

.1	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)*

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? ☒ 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), 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 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 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
Alan J. Meyers	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'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

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

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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)
VARIOUS: UV EXPERT Sunscreen; [redacted]; CAPITAL SOLEIL Sunscreen; ANTHELIOS Sunscreen;

b(4)

ACTIVE INGREDIENT(S)	STRENGTH(S)
Ecamsule	3%
Avobenzone	2%
Octocrylene	10%

RECEIVED
OCT 07 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).
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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	b. Issue Date of Patent	c. Expiration Date of Patent
5,587,150	12/24/1996	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)

Alan J. Meyers
Sr. Vice Vice President
L'Oreal USA Products, Inc.

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

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? N/A ☐ Yes ☐ No

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?	☐ 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)

3.1	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 wavelenths 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 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 this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

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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

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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

EXCLUSIVITY SUMMARY

NDA # 21-501 SUPPL # HFD # 560

Trade Name UV Expert 15, Capital Soleil 15

Generic Name ecamsule/avobenzone/octocrylene

Applicant Name L'Oreal

Approval Date, If Known October 2, 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# 21-502 Anthelios SX (ecamsule, avobenzone, octocrylene)

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:

PEN.820.01, PEN.820.02, 9901.001.COS, PEN.750.02 PEN.910.01, PEN.920.01, PEN.810.01, PEN.810.02

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:

The last four clinical studies (PEN.910.01, PEN.920.01, PEN.810.01, PEN.810.02) were included in NDA 21-502 also but studied different products in separate arms

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"):

PEN.820.01, PEN.820.02, 9901.001.COS, PEN.750.02

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 ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! 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: 10/2/06

Name of Office/Division Director signing form:
Title:

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

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 21-501 **Supplement Type (e.g. SE5):** _____ **Supplement Number:**

Stamp Date: May 16, 2005 **Action Date:** October 2, 2006

HFD-560____ **Trade and generic names/dosage form:** avobenzone, 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:**_____

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.

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 (post-marketing commitment)

Date studies are due (mm/dd/yy): 07/22/09

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 21-501
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)

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/s/

Elaine Abraham
10/30/2006 07:55:44 AM

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)

(Signature)

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

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-501	Efficacy Supplement Type SE-	Supplement Number	
Drug: 3% ecamsule/2% avobenzone/10% octocrylene cream		Applicant: L'Oreal USA Products, Inc.	
RPM: Elaine Abraham		HFD-560	Phone # (301) 796-0843

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.) **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.** (X) Confirmed and/or corrected	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Avobenzone (sunscreen monograph) Octocrylene (sunscreen monograph)

❖ Application Classifications:	
Review priority	(X) Standard ( ) Priority
Chem class (NDAs only)	5
Other (e.g., orphan, OTC)	OTC
❖ User Fee Goal Dates	October 2, 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 4689
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)	
Applicant is on the AIP	( ) Yes (X) No

This application is on the AIP	( ) Yes (X) No
Exception for review (Center Director's memo)	
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	
Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	(X) Verified
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 *N/A-No patents in OB* 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
[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).	
[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). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).*	(X) N/A (no paragraph IV certification) ( ) Verified
[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. Answer the following questions for each paragraph IV certification: Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? (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))). *If "Yes," skip to question (4) below. If "No," continue with question (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)? *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 (3).* Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? (Note: This can be determined by confirming whether the Division has	( ) Yes ( ) No ( ) Yes ( ) No ( ) Yes ( ) No

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.* 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).* 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? (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.*	( ) Yes ( ) No
❖ Exclusivity (approvals only)	
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.)	No
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 #_____ (X) No
Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	6/21/05, 2/24/06, 9/22/06

Check all that apply	
❖ Actions	
Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
Previous actions (specify type and date for each action taken)	AE 3/10/06, AE 7/21/06
Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
Press Office notified of action (approval only)	( ) Yes (X) Not applicable
Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) 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	5/18/06, 7/23/06, 7/10/06, 7/13/06, 8/1/06, 9/20/06
Original applicant-proposed labeling	5/16/05
• 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, 9/25/06
• 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, 2/10/06, 3/23/06, 10/12/06
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 Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	3/6/06, 7/10/06
Clinical Information	
❖ 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 in 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)	10/2/06
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)*	3/2/06
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)*	N/A
❖ 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:

- it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- 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)
- 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.)
- 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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/s/

Elaine Abraham
10/30/2006 08:43:11 AM

RECORD OF TELEPHONE CONVERSATION

Date:	October 12, 2006
Project Manager:	Elaine Abraham
Subject:	clarification of pediatric commitment
NDA:	21-501 (SPF 15), 21-471 (SPF-20)
Sponsor:	L'Oreal
Product Name:	Sunscreens (various trade names)
Phone No:	(732) 680-5562

FDA participant: Elaine Abraham, RPM

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

Background: FDA sent approval letters to NDA 21-501 and 21-471 on October 2 and October 5, 2006, respectively. The letters contained a deferred pediatric post-marketing commitment for the prevention of sunburn in children under 6 months of age. The studies are deferred until July 22, 2009 for NDA 21-501 and October 9, 2009 for NDA 21-471. (L'Oreal has requested waivers of the pediatric studies and these requests are under review.)

Discussion: I called L'Oreal to clarify that safety was the concern in the pediatric studies. L'Oreal stated that they understood that the studies would be safety studies. They noted their waiver requests, but asked, if studies are required, what specific studies would FDA like to have conducted. I responded that if a waiver is not granted, L'Oreal should request a teleconference at that time to discuss more specifically what studies are needed.

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/s/

Elaine Abraham
10/27/2006 08:39:28 AM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: September 14, 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 21-501 labeling comments

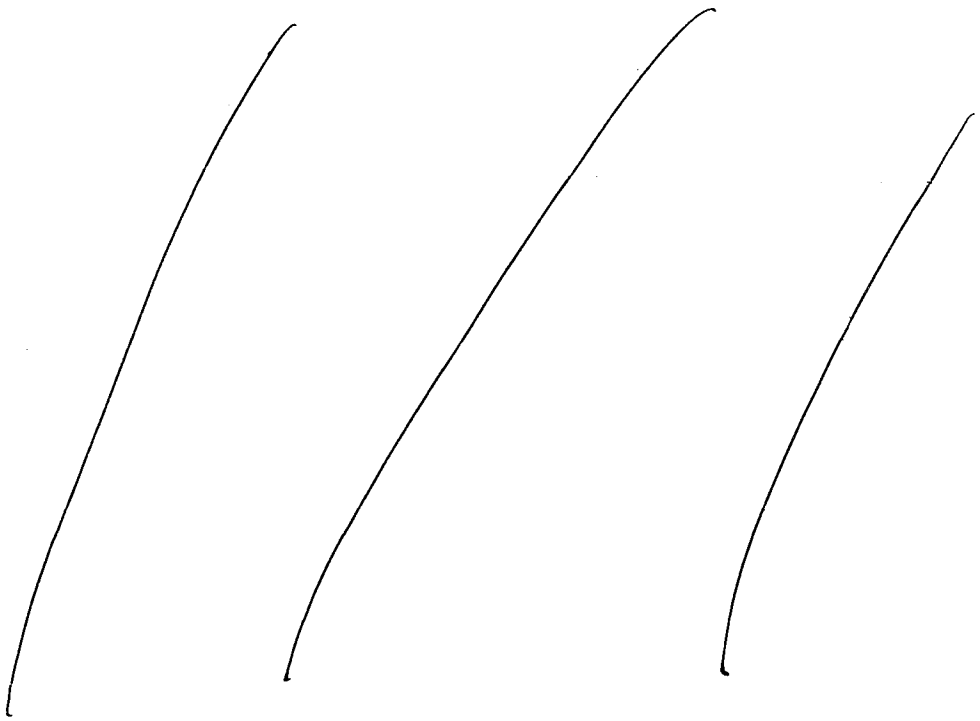
Total no. of pages including cover: 2

Comments:

Document to be mailed: YES X NO

Please refer to your new drug application amendment NDA 21-501 dated August 1, 2006 for your OTC SPF 15 sunscreen products: Vichy CAPITAL SOLEIL 15 and Lancôme UV EXPERT 15.

We have completed our review of your amendment and have the following labeling comments:



In order to ensure a timely action for your new drug application, we request that you respond to the issues listed above as soon as possible by sending revised draft labeling by email or fax, in addition to sending a copy to your NDAs.

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/s/

Elaine Abraham
9/14/2006 08:02:15 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-501

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 acknowledge receipt on August 2, 2006 of your August 1, 2006 resubmission to your new drug application for 2% avobenzone, 3% ecamsule, and 10% octocrylene cream from the following distributors with the following trade names:

- Vichy: CAPITAL SOLEIL 15
- Lancôme: UV EXPERT 15

We consider this a complete, class 1 response to our July 21, 2006 action letter. Therefore, the user fee goal date is October 2, 2006.

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 not fulfilled the requirement for children under the age of 6 months. We are deferring submission of your pediatric studies until July 22, 2009. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of section 2 of the Pediatric Research Equity Act (PREA) within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to

qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. Please note that 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
9/8/2006 05:00:05 PM

RECORD OF TELEPHONE CONVERSATION

Date:	July 24, 2006
Project Manager:	Elaine Abraham
Subject:	safety update question
NDA:	21-501 (SPF 15), 21-471 (SPF-20)
Sponsor:	L'Oreal
Product Name:	Sunscreens (various trade names)
Phone No:	(732) 680-5562

FDA participant: Elaine Abraham, RPM

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

Background: On July 21, 2006, FDA sent an approvable letter to NDA 21-501 because of labeling issues. The letter contained the standard boilerplate paragraph requesting a safety update when the NDA is resubmitted. L'Oreal called me and stated that as there were only minor changes requested in the approvable letter, they would be submitting their amendment shortly. They asked to be released from the safety update requirement. After checking with the ONP medical officer (Daiva Shetty), I called L'Oreal back.

Discussion: I told L'Oreal that as long as the complete response was received within the next one to two months, a safety update would not be required. L'Oreal asked if this would also be true of NDA 21-471. I responded that it would be the same for NDA 21-471.

N.B. The complete response for NDA 21-501 was dated August 1, 2006 and received on August 2, so a safety update is not required. NDA 21-471 was sent an approvable letter on July 25, 2006 because of labeling issues. There was no safety update paragraph in the approvable letter. L'Oreal's complete response was dated August 8, 2006 and received on August 9, so a safety update for NDA 21-471 is not necessary.

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/s/

Elaine Abraham
9/26/2006 10:06:08 AM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: July 18, 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 21-501, 21-502 labeling comments

Total no. of pages including cover: 3

Comments:

Document to be mailed: YES X NO

Please refer to your new drug applications NDA 20-502 and 21-501 dated May 12 and 16, 2005 respectively for your OTC SPF 15 sunscreen products.

(A)

1 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

7 Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

(4)

In order to ensure a timely action for your new drug applications, we request that you respond to the issues listed above as soon as possible by sending revised draft labeling by email or fax, in addition to sending a copy to your NDAs.

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/s/

Elaine Abraham
7/18/2006 02:53:58 PM
CSO

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 21-501, 21-502 information request

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

We reference your NDAs 21-501 and 21-502 and have the following request for information:

b(4)

We are aware that you have submitted an amendment to NDA 21-471 to eliminate [redacted] for Method Number [redacted] Since [redacted] was also proposed in your 4/12/06 amendments of NDAs 21-501 and 21-502, please submit amendments to NDAs 21-501 and 21-502 to eliminate [redacted]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-501
NDA 21-502

DISCIPLINE REVIEW LETTER

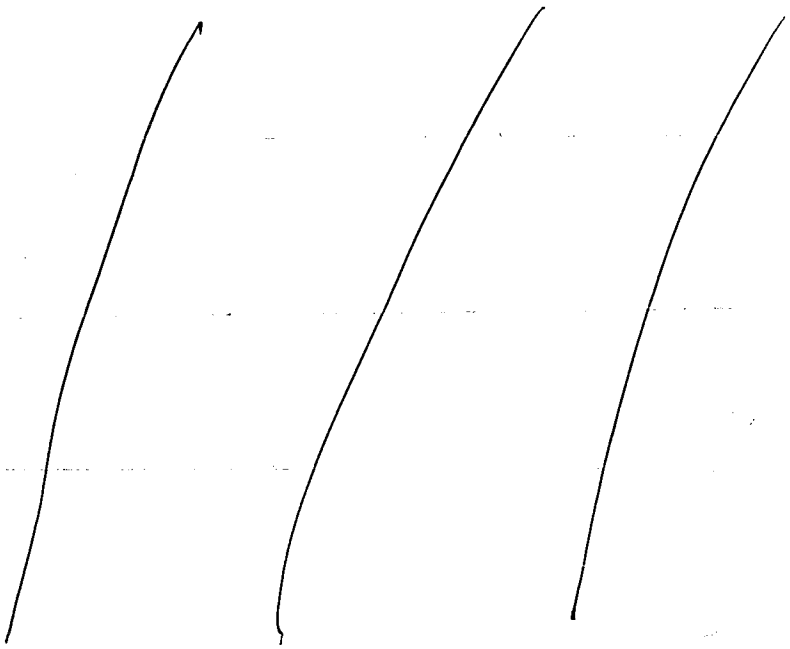
L'Oreal USA Products, Inc.
Attention: Jean R. Grieve
Assistant Vice President, Drug Approval Group
30 L'Oreal Way
Clark, NJ 07066

Dear Ms. Grieve:

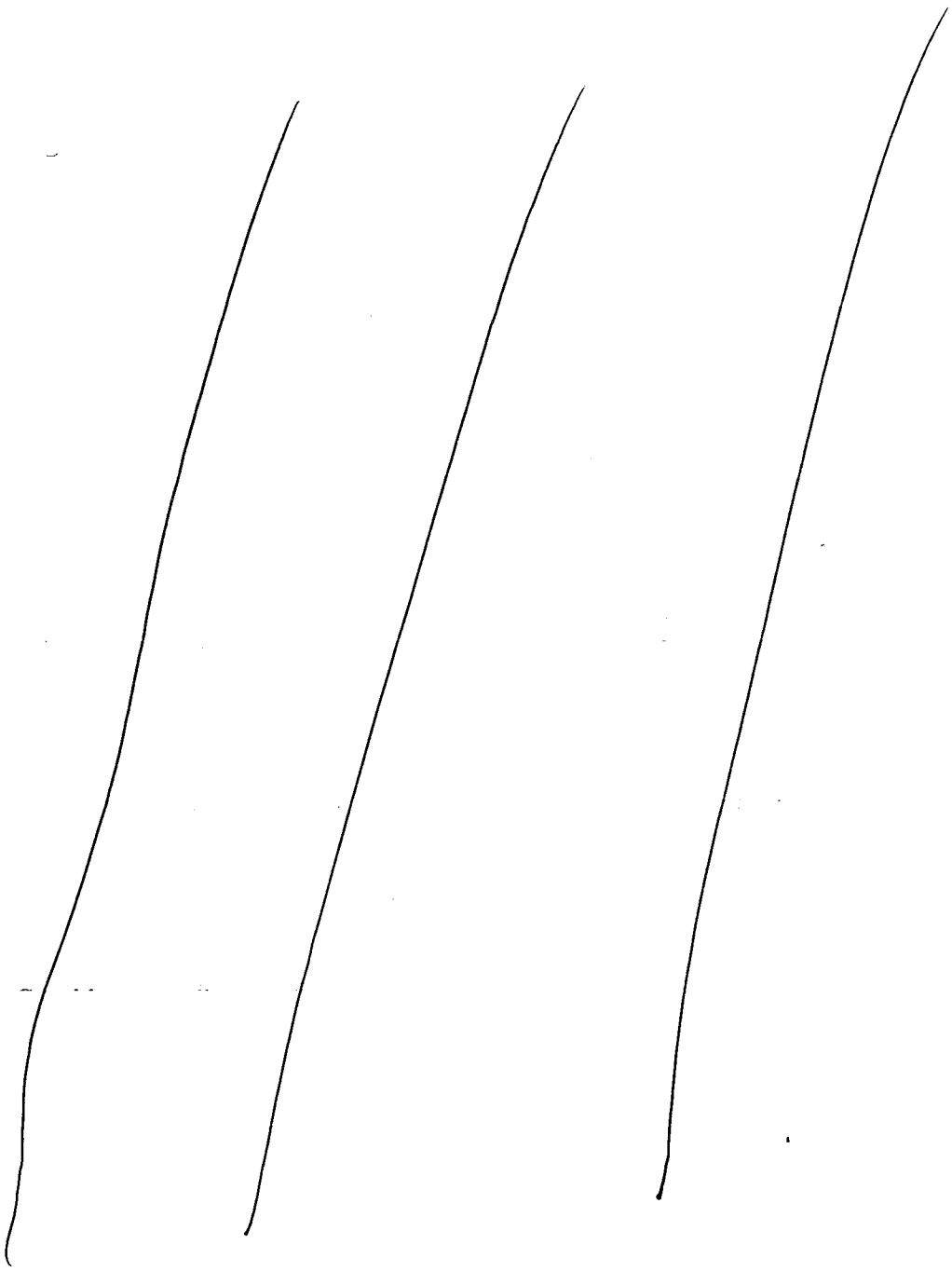
Please refer to your new drug applications (NDA) dated May 16, 2005 (NDA 21-501) and May 12, 2005 (NDA 21-502) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for 2% avobenzone, 3% ecamsule, and 10% octocrylene cream (NDA 21-501), and 2% avobenzone, 2% ecamsule, and 10% octocrylene cream (NDA 21-502).

We also refer to your submission dated May 18, 2006.

Our review of the labeling section of your submission is complete, and we have identified the following deficiencies:



b(4)



b(4)

We are providing these comments to you before we complete our review of the entire applications to give you preliminary notice of issues that we have identified. In conformance

with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your applications. In addition, we may identify other information that must be provided before we can approve these applications. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your applications during this review cycle.

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
6/13/2006 08:41:52 AM

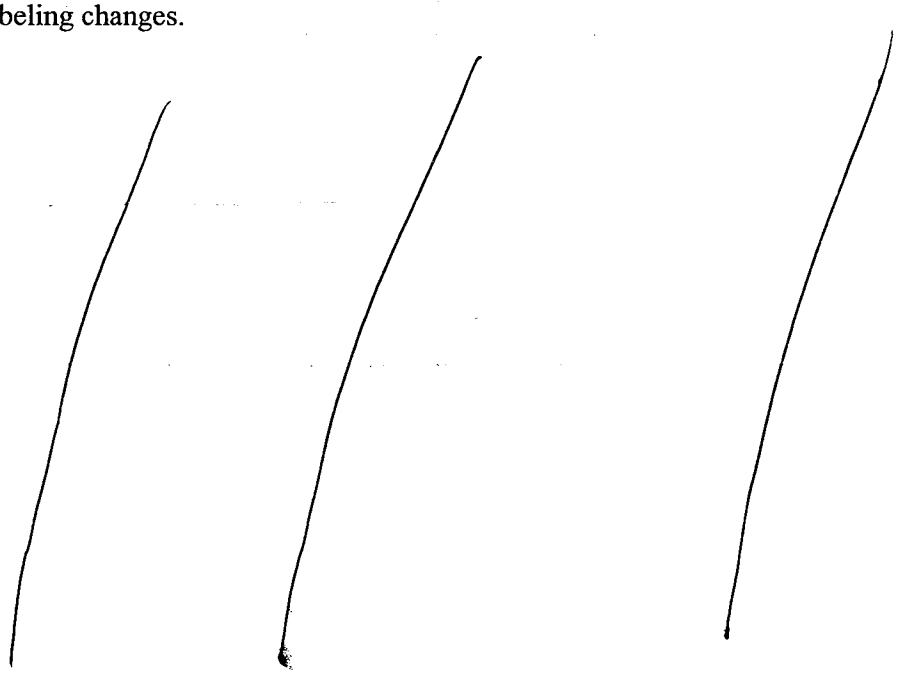
RECORD OF TELEPHONE CONFERENCE

Date:	March 22, 2006
Project Manager:	Elaine Abraham
Subject:	Discuss noncomedogenic claim for sunscreen products
NDA:	21-501, 21-502
Sponsor:	L'Oreal
Product Name:	SPF-15 Sunscreens
Phone No:	(732) 680-5562

FDA participants: Markham Luke, M.D., Acting Director, Division of Dermatology and Dental Products
Daiva Shetty, M.D., Acting Team Leader, Division of Nonprescription Clinical Evaluation (DNCE)
Elaine Abraham, RPM, (DNCE)

L'Oreal participants: Jean Grieve, Assistant VP, R&D, Drug Approval Group
Linda Rhein, Ph.D., Director of Clinical Operations, Drug Approval Group, R&D

Background: FDA sent L'Oreal an approvable letter on March 10, 2006 that contained labeling changes.



b(4)

(B)

1

_____ Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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
5/19/2006 10:50:36 AM
CSO

RECORD OF TELEPHONE CONVERSATION

Date:	February 10, 2006
Project Manager:	Elaine Abraham
Subject:	Discuss chemistry issues
NDA:	21-501, 21-502, 21-471
Sponsor:	L'Oreal
Product Name:	SPF-15 and SPF-20 Sunscreens
Phone No:	(732) 680-5562

FDA participants: Elaine Morefield, Ph.D., Director, Division of Pre-marketing Assessment II
Moo Jhong Rhee, Ph.D., Branch Chief
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead
Sue-Ching Lin, M.S., R.Ph., Chemistry Reviewer
Jane Chang, Ph.D., Chemistry Reviewer
Elaine Abraham, RPM

L'Oreal participant: Jean Grieve, Assistant VP, R&D, Drug Approval Group
Henry Kalinoski, Ph.D., Director, Product Site Support Analytical Chemistry & Microbiology, R & D
Linda Rhein, Ph.D. Director of Clinical Operations, Drug Approval Group, R&D

b(4)

b(4)

(C)

1 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Elaine Abraham
3/10/2006 07:39:44 AM
CSO

RECORD OF TELECONFERENCE

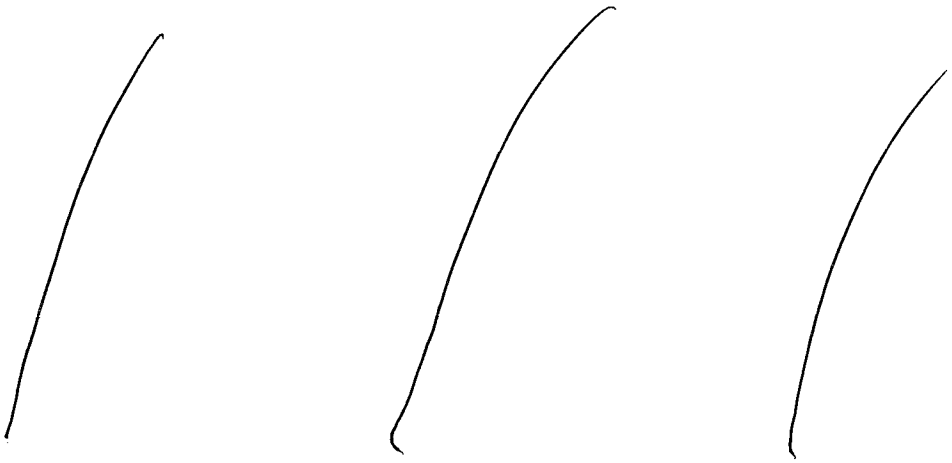
Date:	January 23, 2006
Project Manager:	Elaine Abraham
Subject:	Discuss chemistry issues
NDA:	21-501, 21-502, 21-471
Sponsor:	L'Oreal
Product Name:	SPF-15 and SPF-20 Sunscreens
Phone No:	(732) 680-5562

FDA participants: Moo Jhong Rhee, Ph.D., Branch Chief
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead
Sue-Ching Lin, M.S., R.Ph., Chemistry Reviewer
Jane Chang, Ph.D., Chemistry Reviewer
Elaine Abraham, RPM

L'Oreal participants: Jean Grieve, Assistant VP, R&D, Drug Approval Group
Henry Kalinoski, Ph.D., Director, Product Site Support Analytical Chemistry & Microbiology, R & D

Background: L'Oreal submitted NDAs 21-501 and 21-502 in May 2005 for a 3-ingredient combination sunscreen product. NDA 21-471 was submitted in September 2005 for a 4-ingredient combination sunscreen. Chemistry issues are similar for the three NDAs. This discussion was part of an on-going back and forth between FDA and L'Oreal to resolve outstanding chemistry issues.

Discussion: The following issues and information requests were discussed:



(D)

2 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Elaine Abraham
2/24/2006 02:03:34 PM
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 21-501, 21-502 labeling comments

Total no. of pages including cover: 4

Comments:

Document to be mailed: YES X NO

Please refer to your new drug applications NDA 20-502 and 21-501 dated May 12 and 16, 2005 respectively for your OTC SPF 15 sunscreen products.

(e)

3 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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 21-501, 21-502, 21-471 information request

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

We reference your original NDAs 21-501, 21-502, and 21-471 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 (0.15% for maximum daily dose of >2g).

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
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 21-501

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 16, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for 3% 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 15, 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 21-501 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

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
7/21/05 12:19:01 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

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

FOR FDA USE ONLY

APPLICATION NUMBER
21-501

APPLICANT INFORMATION

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

PRODUCT DESCRIPTION

RECEIVED
OCT 07 2005
CDR/CDER

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)*

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Association of Ecamsule (E), Avobenzone (A) USP, and Octocrylene (O) USP	VARIOUS

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	CODE NAME *(If any)*
Ecamsule: (±)(3E,3'E)-3,3'-(p-phenylenedimethylidyne)bis[2-oxo- 10-boranesulfonic acid	— SPF Water Resistant

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
—	E 3%, A 2%, O 10%	Topical to the Skin

b(4)

(PROPOSED) INDICATION(S) FOR USE:

Preventionof sunburn ; — following — exposure to ultraviolet radiation (UVR)

b(4)

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 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)* ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO APENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ 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)

IND 59,126

b(4)

This application contains the following items: *(Check all that apply)*	
☐	1. Index
☐	2. Labeling *(check one)* ☒ Draft Labeling ☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50 (c))
☐	4. Chemistry section
☐	A. Chemistry, manufacturing, and controls information (e.g.; 21 CFR 314.50(d)(1); 21 CFR 601.2)
☐	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
☐	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
☐	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
☐	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
☐	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
☐	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
☐	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
☐	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
☐	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
☒	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
☐	15. Establishment description (21 CFR Part 600, if applicable)
☐	16. Debarment certification (FD&C Act 306 (k)(1))
☐	17. Field copy certification (21 CFR 314.50 (l)(3))
☐	18. User Fee Cover Sheet (Form FDA 3397)
☐	19. Financial Information (21 CFR Part 54)
☐	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	DATE:
	Jean R. Grieve Assistant Vice President, Drug Approval Group	10/5/05

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
30 L'Oréal Way - Clark, New Jersey 07066	(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:

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

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	TITLE
ALAN J. MEYERS	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

ITEM 18

NDA 21-501
USER Fee # 4689
SPF 15 Water Resistant Sunscreen Lotion

b(4)

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.

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

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

2. TELEPHONE NUMBER *(Include Area Code)*
(732) 680-5562

3. PRODUCT NAME
Mexoryl® SX 15, WR (ecamsule)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
N021501

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☐ YES ☐ 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:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: Pre-Submission.
Note: Partial payments previously made
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER
4689

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ 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.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

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

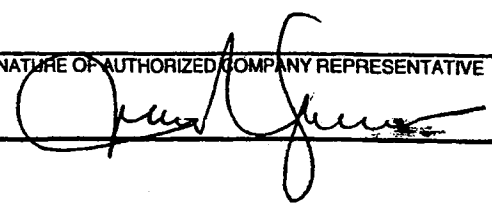
Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments 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

and

Food and Drug Administration
CDER, HFD-94
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	DATE
	Assistant Vice President Drug Approval Group	12/10/04

FORM FDA 3397 (12/03)

PSC Media Arts (301) 443-1090 EF

105245 U.S. FOOD AND DRUG ADMIN. 0001463427 12/07/04

Invoice No.	Description	Date	P.O. No.	Gross Amount	Discount	Net Amount
NDA 21-501	—— SPF	12/3/04	b(4)	$98,500.00	$0.00	$98,500.00
			TOTALS:	$98,500.00	$0.00	$98,500.00

b(4)

NDA USER FEE

SPF 15 WR

L'OREAL USA, INC.

PLEASE DETACH THIS REMITTANCE ADVICE BEFORE DEPOSITING CHECK

L'ORÉAL USA, Inc.
CLARK, NJ 07066

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

62-26/311 121344 NO. 0001463427

RESEARCH & DEVELOPM DATE 12/7/04 CHECK NO. 0001463427 AMOUNT $ *****98,500.00

PAY *NINETY EIGHT 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 NO 21 501
USER FEE ID NUMBER 4689

AUTHORIZED SIGNATURE

VOID VOID VOID

⑈0001463427⑈ ⑆031100267⑆ 6301455618 509⑈

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004.

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

2. TELEPHONE NUMBER *(Include Area Code)*

(732) 680-5562

3. PRODUCT NAME

Mexoryl® SX 15, WR (ecamsule)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

NO 21501

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☐ YES ☐ 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:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

Note: NDA User Fee Payment
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4689

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

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ 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.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS 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

and

Food and Drug Administration
CDER, HFD-94
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	DATE
[signature]	Assistant Vice President Drug Approval group	12/19/03

FORM FDA 3397 (1/03)

PSC Media Arts (301) 443-1090 EF

106245 U.S. FOOD AND DRUG ADMIN.

CHECK NUMBER 0001299470

DATE 12/18/03

Invoice No.	Description	Date	P.O. No.	Gross Amount	Discount	Net Amount
121603USF5735000	NDA21501	12/16/03		$573,500.00	$0.00	$573,500.00
			TOTALS:	$573,500.00	$0.00	$573,500.00

b(4)

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L'OREAL USA, INC.

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CLARK, NJ 07066

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

62-26/311 9054-3

NO. 0001299470

RESEARCH & DEVELOPM

DATE 12/18/03 CHECK NO 0001299470

AMOUNT $ *****573,500.00

PAY *FIVE HUNDRED SEVENTY-THREE THOUSAND FIVE HUNDRED DOLLARS AND 00 CENTS* Dollars

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

NDA Number NO 21501
User Fee ID Number 4689

AUTHORIZED SIGNATURE

VOID

⑈0001299470⑈ ⑆031100267⑆ 6301455618 509⑈