

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-471**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

**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.

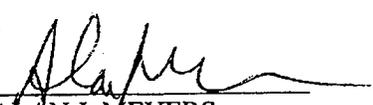
(2) Applicant refers to 21 C.F.R. § 314.108(b)(2) in support of this claim.

(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:

9/16/2005

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

21-471

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: SOLAR EXPERTISE Sunscreen: ANTHELIOS Sunscreen:

ACTIVE INGREDIENT(S)

ecamsule  
titanium dioxide  
avobenzone  
octocrylene

STRENGTH(S)

2%  
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.

**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  
Asnières

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)

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)

Norman H. Stepno, Esquire  
Burns, Doane, Swecker & Mathias LLP

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

Yes

No

H, 585, 577

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?  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)**

- 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) **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 Meyers*

9/16/2005

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

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.

## INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://forms.psc.gov/forms/foia.htm>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

##### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

##### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

##### 4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

- 4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

##### 5. No Relevant Patents

Complete this section only if applicable.

##### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

**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

21-471

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; SOLAR Expertise Sunscreen; CAPITAL Soleil Sunscreen; ANTHELIOS Sunscreen

ACTIVE INGREDIENT(S)

Ecamsule  
Titanium Dioxide  
Avobenzone  
Octocrylene

STRENGTH(S)

2%  
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.*

*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

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)

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

5,587,150

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

N/A

Yes

No

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?  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 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 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 Meyers*

9/16/2005

**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.*

## INFORMATION AND INSTRUCTIONS FOR FORM 3542a

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

#### General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
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- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://forms.psc.gov/forms/fdahm/fdahm.htm>.

#### First Section

Complete all items in this section.

##### 1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

##### 2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

##### 3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

##### 4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

- 4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

##### 5. No Relevant Patents

Complete this section only if applicable.

##### 6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

## EXCLUSIVITY SUMMARY

NDA # 21-471

SUPPL #

HFD # 560

Trade Name UV Expert 20, Capital Soleil 20, Anthelios 20, UV Protective Suncare

Generic Name ecamsule/avobenzone/octocrylene/titanium dioxide

Applicant Name L'Oreal

Approval Date, If Known October 5, 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# 21-501 (ecamsule, avobenzone, octocrylene)

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.810.03, PEN.810.04, PEN.750.03, PEN.820.01, PEN.820.02,  
PEN.910.01, PEN.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:

The last four clinical studies (PEN.820.01, PEN.820.02, PEN.910.01, PEN.920.01) were included in NDA 21-501 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.810.03, PEN.810.04, PEN.750.03

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: 10/5/06

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 #: 21-471 Supplement Type (e.g. SE5): \_\_\_\_\_ Supplement Number: \_\_\_\_\_

Stamp Date: May 16, 2005 Action Date: October 5, 2006

HFD-560 \_\_\_\_\_ Trade and generic names/dosage form: avobenzone, ecamsule, octocrylene, and titanium dioxide 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): 10/9/09

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

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Elaine Abraham  
10/30/2006 07:59:29 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.

September 12, 2005  
(Date)

Jean Grieve  
(Signature)

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

# 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).

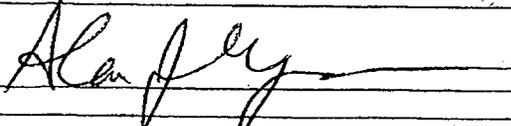
Please mark the applicable checkbox.

- (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 of Investigators for NDA 21-471.

- (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 9/16/05

### 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

**FINANCIAL DISCLOSURES FOR CLINICAL INVESTIGATORS FOR NDA 21-471 –  
COVERED STUDIES**

Financial disclosures were obtained for investigators from the following studies identified that are directly related to the safety and efficacy assessments or are considered supportive of the safety and efficacy of the \_\_\_\_\_ SPF 20 Water Resistant Sunscreen Lotion (539-106) and its related formulations.

The Phase 3 efficacy studies that directly evaluate \_\_\_\_\_ SPF 20 Water Resistant Sunscreen Lotion are:

- PEN.820.01, PEN.820.02, PEN.810.03, PEN.810.04, PEN.910.01 and PEN.920.01

The Phase 2 efficacy studies that support compliance with FDA's OTC sunscreen requirement for combination products are:

- PEN.810.05, PEN.810.06, and PEN.910.02

Supportive studies that provide additional evidence of efficacy are:

- PEN.810.01, PEN.810.02, 99001.01.COS, 1.CG.03.SRE.2612, 1.CG.03.SRE.2613, 1.CG.03.SRE.2614, 1.GUS.05.SRE.18045.R01, 1.GUS.05.SRE.2639, RD.06.SRE.2616, RD.06.SRE.18057

The Phase 1 safety studies that directly evaluate \_\_\_\_\_ SPF 20 Water Resistant Sunscreen Lotion are:

- PEN.110.01, PEN.210.01, and PEN.250.01

The Phase 3 safety studies and supportive studies that provide additional evidence of safety are:

- PEN.750.01, PEN.750.02, PEN.750.03, RD.06.SRE.18047, PEN.570.01, PEN.570.02

Supportive Pediatric use Cosmetic studies that provide additional evidence of safety are:

- IK 177- IK 177 bis/Ecut 04010- Ecut 04010 bis, IK 181/Ecut 04011, IK 182/Ecut 04012, IK 335/Ecut 04017, EF PK030mod/Ecut 04013, PK 031/Ecut 04014, IEUT 03058, IEUT 03066, IEUT 03074, IEUT 04004, IEUT 04005, IEUT 04052, IEUT 04053, IEUT 04026

17 Page(s) Withheld

X Trade Secret / Confidential

       Draft Labeling

       Deliberative Process

## 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.

APPEARS THIS WAY  
ON ORIGINAL



# OTC Drug Labeling Review Addendum for L'Oreal Sunscreens (NDA 21-471)

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

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**SUBMISSION DATES:** August 8 and  
September 22,  
2006

**RECEIVED DATES:** August 9 and  
September 25, 2006

**REVIEW DATE:** October 4, 2006

**NDA/SUBMISSION TYPE:** NDA 21-471

**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:**

- Vichy CAPITAL SOLEIL 20
- Lancôme UV EXPERT 20
- Kiehl's UV PROTECTIVE SUNCARE
- La Roche-Posay ANTHELIOS 20

**ACTIVE INGREDIENTS:**

- Avobenzone, 2%
- Ecamsule —
- Octocrylene, 10%
- Titanium dioxide, 2%

**INDICATIONS:** Helps prevent sunburn; provides broad spectrum protection from UVA and UVB radiation

**PHARMACOLOGICAL CATEGORY:** Sunscreen (broad spectrum)

**LABELING SUBMITTED:** Tube & carton labels for the following 3.4 oz

products:

- Vichy CAPITAL SOLEIL 20
- Lancôme UV EXPERT 20
- Kiehl's UV PROTECTIVE SUNCARE
- La Roche-Posay ANTHELIOS 20

**REVIEWER:**

Michael L. Koenig, Ph.D.

**BACKGROUND**

In response to a July 25, 2006, approvable letter recommending changes to the labeling for this NDA (21-471), the sponsor submitted revised labeling for the following products on August 8, 2006:

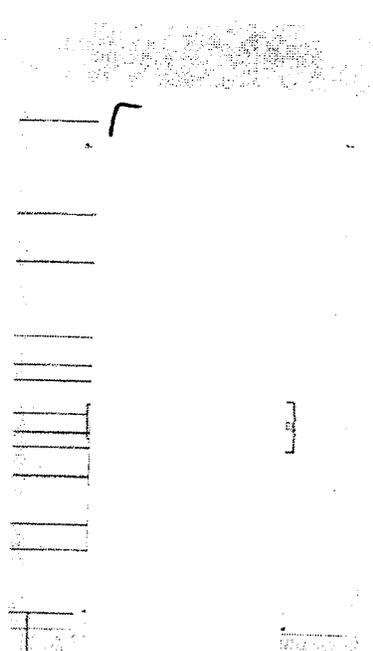
- Vichy CAPITAL SOLEIL 20
- Lancôme UV EXPERT 20
- Kiehl's UV PROTECTIVE SUNCARE
- La Roche-Posay ANTHELIOS 20

The sponsor did not submit revised labeling for L'Oreal SOLAR EXPERTISE 20, noting that it intends to submit labeling for this product as a supplement to the approved NDA.

FDA reviewed the submitted labeling and informed the sponsor by FAX on September 14, 2006, that revisions would be necessary. The sponsor made the recommended revisions and resubmitted the labeling to FDA on September 22, 2006.

**REVIEWED LABELING**

**Vichy Tube - Front**



11 Page(s) Withheld

       Trade Secret / Confidential

X Draft Labeling

       Deliberative Process

## La Roche-Posay Carton – Right

## REVIEWER'S COMMENTS

1. The trade names for these products are distinct from other sunscreen drug products included under NDAs 21-501 and 21-502. Three of the four products include the SPF value (20) as part of the trade name. The other product (UV PROTECTIVE SUNCARE) includes a unique trade name modifier (SUNCARE). These trade names are acceptable.

Distributor	NDA 21-471	NDA 21-501	NDA 21-502
Vichy	CAPITAL SOLEIL 20	CAPITAL SOLEIL 15 <sup>AP</sup>	UV ACTIV
Lancôme	UV EXPERT 20	UV EXPERT 15 <sup>AP</sup>	UV EXPERT 15
Kiehl's	UV PROTECTIVE SUNCARE		UV PROTECTIVE
La Roche Posay	ANTHELIOS 20		ANTHELIOS SX <sup>AP</sup>
Shu Uemura			UV DEFENDER

<sup>AP</sup> Approved

2. The sponsor has separated statements about the effects of UV exposure from product claims. For example, statements that UVA rays may contribute to skin aging appear in separate (but adjacent) paragraphs from claims that these products provide protection against UVA radiation. This is acceptable because it sufficiently avoids an implied claim that the product helps prevent premature skin aging.

3. In its August 8 submission, the sponsor made all of the changes to tube and carton labeling requested by FDA in the approvable letter dated July 25, 2006. On September 14, 2006, FDA informed the sponsor that additional labeling changes were required. In a September 22, 2006, response, the sponsor made the following changes to the labeling submitted on August 8, 2006:
- modified text implying that UVA rays alone are responsible for skin aging by appending the statement "UVB rays may also contribute to premature skin aging."
  - changed word or phrases implying that these products are superior to other OTC sunscreen drug products
  - changed the bulleted statement under Directions that read \_\_\_\_\_ to "reapply after 40 minutes of swimming or perspiring and after towel drying."
  - removed the phrase "FACE AND BODY" that appeared between the proprietary name "UV PROTECTIVE SUN CARE" and the statement of identity "SUNSCREEN CREAM" and moved the phrase "SUNSCREEN CREAM" so that it is directly adjacent to the phrase "UV PROTECTIVE SUN CARE"
  - revised the statement of identity ("SUNSCREEN CREAM") on the La Roche-Posay tube and carton front panels so that is more prominently displayed in black ink
  - acknowledged the contribution of the active ingredient titanium dioxide in text and graphics depicting the coverage of other active ingredients

These changes are acceptable.

4. In its September 22, 2006, response, the sponsor made the following *additional* changes to the labeling submitted on August 8, 2006:
- added the sentence "The skin is protected, moisturized, and healthy-looking." as the last sentence in paragraph 2 on the Vichy carton back panel
  - deleted paragraph 1 on the Lancôme carton left side panel and replaced it with two new paragraphs
  - changed descriptor "Body Protection" to "Face Protection" on the Lancôme tube and carton front panels and bottom flap of carton

These changes are acceptable.

5. The sponsor also added the bulleted statement "Oil-Free" to the bulleted text on the Lancôme carton left side panel. Following discussion with the CMC reviewer, this reviewer believes it is incorrect to refer to this formulation as "oil-free." The CMC reviewer noted that this product contains cyclomethicone and dimethicone oils as components of the cream base and stated that the term "non-greasy" is more appropriate.
6. This reviewer concurs with Dr. Ganley in his assertion that consumers might mistakenly assume that sunscreen products marketed as daily (or 24-hour) moisturizers need only be applied once daily (for UV protection). The sponsor must comply with the requirement that any proposal to increase the package size of these products necessitates submission of a prior approval supplement (Office Director's memo filed under NDA 21-502 on July 21, 2006).

**RECOMMENDATIONS**

1. Send an approval letter for the 3.4 oz. (100 g) product by the following distributors with the following trade names:
  - Vichy CAPITAL SOLEIL 20
  - Lancôme UV EXPERT 20
  - Kiehl's UV PROTECTIVE SUNCARE
  - La Roche-Posay ANTHELIOS 20

2. Note that, per the sponsor's October 4, 2006 request, ANTHELIOS 20 distributed by LaRoche-Posay is designated as the reference listed drug for this application.
3. In the approval letter, inform the sponsor that the application is approved for use as recommended in the agreed-upon labeling text and with the minor editorial revision listed below. This change can be made at the time of next printing or at 180 days, whichever occurs earlier.

Replace the phrase "oil-free" with the term "non-greasy" in every occurrence on the labels.

The final printed labeling (FPL) must include the revision listed above, be otherwise identical to the tube and carton labels submitted September 22, 2006, and must be in the "Drug Facts" format (21 CFR 201.66).

4. In the approval letter, inform the sponsor that, if it intends to market this product under additional labeling (e.g., under a different trade name) or increase the package size from 3.4 oz. (100 g), it must submit a prior approval supplement.

**APPEARS THIS WAY  
ON ORIGINAL**

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this page is the manifestation of the electronic signature.**  
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/s/

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Michael Koenig  
10/4/2006 08:56:03 AM  
INTERDISCIPLINARY

Matthew Holman  
10/4/2006 12:20:17 PM  
INTERDISCIPLINARY



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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** September 14, 2006

<b>To:</b> Jean Grieve	<b>From:</b> Elaine Abraham Project Manager
<b>Company:</b> L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
<b>Fax number:</b> (732) 909-2007	<b>Fax number:</b> (301) 796-9899
<b>Phone number:</b> (732) 680-5562	<b>Phone number:</b> (301) 796-0843
<b>Subject:</b> NDA 21-471 labeling comments	

**Total no. of pages including cover:** 3

**Comments:**

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**Document to be mailed:**                      YES                       NO

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Please refer to your new drug application amendment NDA 21-471 dated August 8, 2006 for your OTC SPF 20 sunscreen products: Vichy CAPITAL SOLEIL 20, Lancôme UV EXPERT 20, Kiehl's UV PROTECTIVE SUNCARE, and La Roche Posay ANTHELIOS 20.

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

1. Change text implying that UVA rays alone are responsible for skin aging (i.e., "the aging of the skin," or "the appearance of age spots"). UVB rays may also contribute to skin aging. It is acceptable to note that UVB rays also contribute to skin aging in an adjoining sentence or paragraph (e.g., La Roche-Posay secondary carton back panel). The following labels require revision:
  - Vichy tube and carton back panels
  - Vichy carton right side panel
  - Lancôme carton right side panel
  - Kiehl's carton back panel
  
2. Change words or phrases implying that these products are superior to other sunscreen drug products. Because no comparative studies were submitted, such claims are unsubstantiated. This revision must be made to the following labels:
  - Vichy tube and carton back panels: "\_\_\_\_\_ " and \_\_\_\_\_
  
  - Lancôme carton left side panel: \_\_\_\_\_
  
3. Change the statement under *Directions* that reads, \_\_\_\_\_ . Because this product is water resistant, the statement should read, "Reapply after 40 minutes of swimming or perspiring and after towel drying." This revision must be made to the following labels:
  - Vichy tube back panel
  - Vichy carton left side panel
  - Lancôme tube and carton back panels
  - Kiehl's tube back panel
  - Kiehl's carton left side panel
  - La Roche-Posay tube back panel
  - La Roche-Posay carton left side panel
  
4. Remove the phrase "FACE AND BODY" that appears between the proprietary name "UV PROTECTIVE SUN CARE" and the statement of identity "SUNSCREEN CREAM." Move the phrase "SUNSCREEN CREAM" so that it is directly adjacent to the phrase "UV PROTECTIVE SUN CARE." The statement of identity must be in direct conjunction with the proprietary name (21 CFR 201.61(b)).
  
5. Revise the statement of identity ("SUNSCREEN CREAM") on the La Roche-Posay tube and carton front panels so that is more prominently displayed in accordance

with the intent of 21 CFR 201.61(b). This can be done by changing the font color from orange to black.

6. When describing the protection provided by avobenzone, ecamsule, and octocrylene (e.g., the graph with umbrellas), you must also describe the protection provided by titanium dioxide:
  - Lancome secondary carton right side panel
  - Kiehl's and La Roche-Posay secondary carton back panels

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/

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Elaine Abraham  
9/14/2006 07:59:51 AM  
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-471

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 9, 2006 of your August 8, 2006 resubmission to your new drug application for 2% avobenzone, 2% ecamsule, 10% octocrylene and 2% titanium dioxide cream from the following distributors with the following trade names:

- Vichy: CAPITAL SOLEIL 20
- Lancôme: UV EXPERT 20
- Kiehl's: UV PROTECTIVE SUNCARE
- La Roche Posay: ANTHELIOS 20

We consider this a complete, class 1 response to our July 25, 2006 action letter. Therefore, the user fee goal date is October 9, 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 October 9, 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

NDA 21-471

Page 2

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](http://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,

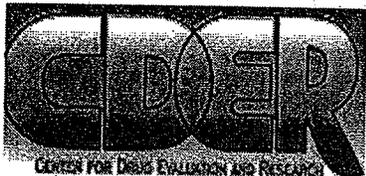
*{See appended electronic signature page}*

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/

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Leah Christl  
9/11/2006 09:12:20 AM



# OTC Drug Labeling Review for L'Oreal SPF 20 Sunscreens (NDA 21-471)

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

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**SUBMISSION DATE:** September 27, 2005    **RECEIVED DATE:** September 28, 2005

**REVIEW DATE:** July 21, 2006

**NDA/SUBMISSION TYPE:** 21-471 (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:** SPF 20 Water Resistant Sunscreen Cream

**ACTIVE INGREDIENTS:** Avobenzone, 2%  
Ecamsule, 2%  
Octocrylene, 10%  
Titanium Dioxide, 2%

**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:** Tube & carton labels for 100 mL (3.4 fl. oz.):  
• Vichy CAPITAL SOLEIL  
• LaRoche-Posay ANTHELIOS  
• Lancome UV EXPERT  
• L'Oreal SOLAR EXPERTISE

**REVIEWER:** Michael L. Koenig, Ph.D.

**TEAM LEADER:** Matthew Holman, Ph.D.

## BACKGROUND

The sponsor submitted labeling for a single sunscreen marketed to be marketed under four trade names. These trade names are identical to some of those under NDA 21-501.

## REVIEWER'S COMMENTS

1. The four trade names are acceptable as proposed. They are identical to trade names approved for NDA 21-501 except without the modifier (i.e., without "15" at end of trade name). According to DMETS, the sunscreens containing four active ingredients under NDA 21-471 must have a different trade name than the sunscreens containing three active ingredients under NDAs 21-501 and 21-502. Thus, the proposed trade names are acceptable. However, the sponsor may wish to include the trade name modifier "20" to further distinguish the SPF 15 sunscreens from the SPF 20 sunscreens.
2. The sponsor must make the revisions to the labeling consistent with the following communications from FDA to the sponsor for NDAs 21-501- and 21-502:
  - February 22, 2006, facsimile
  - March 11, 2006, approvable (AE) letter
  - June 13, 2006, discipline review letter
  - July 18, 2006, discipline review letter

The following revisions must be made to all products under the NDA:

- a. Eliminate terminal zeros in expressions of the percentage of each active ingredient present. Consumers may overlook decimal points and, thus, misread the percentage of each active ingredient present.
- b. In *Uses*, delete the phrase \_\_\_\_\_  
\_\_\_\_\_ from the bulleted statement \_\_\_\_\_  
\_\_\_\_\_
- c. Remove the term \_\_\_\_\_ for all labels. The term is not allowed in sunscreen labeling because UVA testing procedures and corresponding labeling have not yet been defined under the sunscreen monograph. You may include the claim "broad spectrum" or "provides" (select one of the following: "UVB and UVA" or "broad spectrum") "protection" outside the Drug Facts box.
- d. In *Warnings*, add the following warning: "Do not use on [bullet] broken skin [bullet] serious burns." This warning is necessary because (1) application to broken or

burned skin is likely to increase systemic absorption and (2) submitted safety studies reflect use only on intact skin.

- e. Revise the statement of identity (i.e., "sunscreen") so that it appears in bold face type on the principal display panel (PDP) and in a size reasonably related to the most prominent printed matter on the PDP, in accordance with § 201.61(c). In addition, you may want to increase the font size of the following statements in order to enhance consumer awareness of important information:
- "Water Resistant"
  - "SPF 20"
- f. Remove the following terms from all primary and secondary container labeling:
- \_\_\_\_\_
  - \_\_\_\_\_
  - "\_\_\_\_\_"
- Consumers may interpret these terms as superiority claims. Such claims are unsubstantiated.
- g. Remove statements identifying these products as \_\_\_\_\_ and/or "\_\_\_\_\_". The submitted studies do not support the claim.
- h. Remove claims that these products are "\_\_\_\_\_" or "\_\_\_\_\_." No data was submitted to support these claims.
- i. Revise the dosage form from \_\_\_\_\_ to "cream."
- j. Revise any statements indicating the product \_\_\_\_\_ against UV damage so that the statements indicate the product "helps protect."
- k. Remove any reference to UVA radiation as the "skin-aging" UV radiation, including reference to wrinkling, fine lines, age spots, etc. Both UVB and UVA radiation contribute to premature skin aging.
- l. Remove or revise statements indicating that UVA rays cause \_\_\_\_\_ FDA is not aware of definitive evidence from the literature supporting these statements.
- m. To prevent consumer confusion, include the USAN name "ecamsule" wherever the trademark name "Mexoryl SX" appears. Similarly, include the USP name "avobenzonone" wherever the registered name "Parsol" appears.
- n. Remove the statement \_\_\_\_\_ "FDA's Division of Medication Errors and Technical Support contends that this statement is promotional. The statement may imply a superiority claim (over sunscreens that do not contain this statement), even though data has not been submitted to substantiate a superiority claim."

- o. Remove the statement "\_\_\_\_\_ No data were submitted to support this claim.
- p. Remove the statement "\_\_\_\_\_ " from the following Vichy PDP statement:  
BROAD SPECTRUM  
UVA/UVB PROTECTION  
\_\_\_\_\_
- q. Revise labeling implying that a product provides \_\_\_\_\_ protection. No data were submitted to support this claim.

### RECOMMENDATIONS

Send an approvable (AE) letter to the sponsor for the following distributors and trade names:

- Vichy CAPITAL SOLEIL
- LaRoche-Posay ANTHELIOS
- Lancome UV EXPERT
- L'Oreal SOLAR EXPERTISE

In the AE letter, identify the labeling deficiencies as those listed under REVIEWER'S COMMENTS in this review.

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/s/

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Matthew Holman  
7/25/2006 02:07:43 PM  
INTERDISCIPLINARY

## 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.



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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** July 18, 2006

<b>To:</b> Jean Grieve	<b>From:</b> Elaine Abraham Project Manager
<b>Company:</b> L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
<b>Fax number:</b> (732) 909-2007	<b>Fax number:</b> (301) 796-9899
<b>Phone number:</b> (732) 680-5562	<b>Phone number:</b> (301) 796-0843
<b>Subject:</b> NDA 21-501, 21-502 labeling comments	

**Total no. of pages including cover:** 3

**Comments:**

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**Document to be mailed:**                      YES                      X NO

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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.

We have completed our review and have the following labeling comments:

1. Indication/Promotional Uses Statement - All Products

a. All instances of the indication \_\_\_\_\_

\_\_\_\_\_ must be changed to  
"helps provide protection from UVA rays" ("UVA and UVB rays" or "both short  
and long wavelength UVA radiation").

This change must be made in each Uses section and in places where the indication  
statement is used as a promotional statement (e.g., "Capital Soleil 15 with Mexoryl  
SX helps provide protection from UVA rays..." on the secondary mechanical back  
panel).

- b. If the promotional statement uses any other skin effect in place of "skin damage and  
premature aging of the skin," the text regarding skin effects must be deleted. There  
is a single exception, that you may state in promotional text that "UVA and UVB"  
or "UVB" helps protect against "sunburn."

2. Kiehl's Promotional Text

The 5 sentence paragraph containing promotional text on the Kiehl's products must  
be modified (i.e., the text that begins " \_\_\_\_\_ ..." and ends

The second sentence, \_\_\_\_\_", should be removed  
from the paragraph.

This sentence may be used if 1) it appears after the paragraph discussed above, 2) is  
separated from the previous paragraph by a blank line, and 3) is followed by the  
sentence "It is important to decrease UV exposure by limiting time in the sun,  
wearing protective clothing, and using a sunscreen."

3. Vichy Promotional Statement

The front label text which reads:

"BROAD SPECTRUM  
UVA/UVB PROTECTION  
\_\_\_\_\_

must be modified to read:

**“BROAD SPECTRUM  
UVA/UVB PROTECTION”**

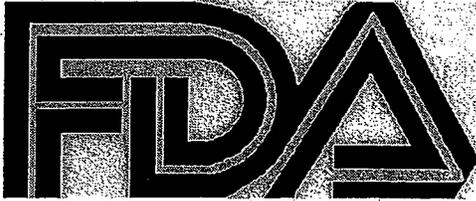
In order to ensure a timely action for your new drug applications, we request that you respond to the issues listed above as soon as possible by sending revised draft labeling by email or fax, in addition to sending a copy to your NDAs.

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/s/

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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

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## FACSIMILE TRANSMITTAL SHEET

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DATE: May 23, 2006

<b>To:</b> Jean Grieve	<b>From:</b> Elaine Abraham Project Manager
<b>Company:</b> L'Oreal USA Products	Division of Nonprescription Clinical Evaluation Office of Nonprescription Products
<b>Fax number:</b> (732) 909-2007	<b>Fax number:</b> (301) 796-9899
<b>Phone number:</b> (732) 680-5562	<b>Phone number:</b> (301) 796-0843
<b>Subject:</b> NDA 21-471 information request	

Total no. of pages including cover: 2

Comments:

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Document to be mailed:	YES	NO
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We reference your original NDA 21-471 and have the following request for information:

Revise the calculation in analytical method \_\_\_\_\_ ) to eliminate the use of the conversion factor, Q, for ecamsule impurities. The calculation should be:

$$\% \text{ impurity} = \frac{R_{\text{imp}}}{R_{\text{std}}} \times \frac{W_{\text{std}} \times P_{\text{std}}}{V_{\text{std}}} \times D_{\text{std}} \times \frac{V_{\text{sam}}}{W_{\text{sam}}} \times \frac{100}{\text{LC}} \times \frac{1}{\text{RRF}}$$

Where:

$R_{\text{std}}$	=	Mean peak area response of active in bracketing standard injections
$R_{\text{imp}}$	=	Peak area response of impurity in the sample injection
$W_{\text{std}}$	=	Weight of active in standard (mg)
$P_{\text{std}}$	=	Purity of active in standard (decimal) – [See Note 1 below]
$V_{\text{std}}$	=	Volume of standard solution (mL)
$W_{\text{sam}}$	=	Weight of sample (g)
$V_{\text{sam}}$	=	Volume of sample solution (mL)
$D_{\text{std}}$	=	Dilution of standard solution (volume pipeted/volume final X volume pipeted/volume final)
RRF	=	Relative response factor: see section J
100	=	Conversion to percent
LC	=	Label claim (mg/g)

Note:

1. For the ecamsule standard purity, apply a correction factor of 0.65 (i.e.,  $P \times 0.65$ ) to account for the ecamsule : \_\_\_\_\_.

The application of "Q" in the calculation resulted in ecamsule impurities being reported only 1/3 of the actual levels. Ecamsule impurities are calculated relative to the ecamsule content in the drug product. It is irrelevant to the fact that the drug substance is supplied in \_\_\_\_\_.

Please respond by May 25 so that we have adequate time to review your application prior to the action due date.

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**MEMORANDUM  
SERVICES**

DEPARTMENT OF HEALTH AND HUMAN

Public Health Service  
Food and Drug Administration  
Center For Drug Evaluation and Research

DATE: April 25, 2006

FROM: Jean Temeck, M.D.  
Acting Team Leader  
Division of pediatric Drug Development

THROUGH: Lisa Mathis, M.D.  
Acting Division Director  
Division of Pediatric Drug Development

TO: Andrea Leonard-Segal  
Acting Division Director  
Division of Nonprescription Clinical Evaluation

NDA/PRODUCT: NDA: 21-471: ~~SPF 20 Water Resistant (WR)~~  
Sunscreen Lotion

SPONSOR: L'Oreal USA Products

SUBJECT: Determination of the need for pediatric studies in children  
less than 6 months of age versus partial waiver for ~~SPF 20 Water Resistant~~  
Sunscreen Lotion.

**Background**

On September 27, 2005, the Sponsor submitted nonclinical and clinical studies with ~~SPF 20 WR Sunscreen Lotion~~ for review to FDA, the Division of Nonprescription Clinical Evaluation. On February 1, 2006, they submitted their 120-day safety update report as required by 21 CFR 314.50 to the Review Division. This NDA, including the safety update is under review by the Division of Nonprescription Clinical Evaluation. On April 24, 2006, the Review Division submitted a copy of the summary section of the safety update and its appendix 2 to the Division of Pediatric Drug Development (DPDD).

~~SPF 20 Water Resistant Sunscreen Lotion~~ contains 4 active ingredients: 10% octocrylene, 2% avobenzone, 2% titanium dioxide and 2% ecamsule. The first 3 ingredients are approved under the final OTC sunscreen monograph. The fourth, ecamsule, is a new molecular entity that has not been previously marketed in the United States although it has been marketed in Europe and other parts of the world since 1993.

The Division of Pediatric Drug Development (DPDD) was previously consulted by the Review Division regarding similar sunscreen products, ~~SPF 15 WR Lotion and SPF 15 Lotion~~ to determine the need for conduct of pediatric studies in infants less than 6 months of age. Neither of these products contain titanium dioxide and the concentration of ecamsule is 3% in the SPF 15 WR Lotion and 2% in the SPF 15 Lotion. Based on acknowledgement by the American Academy of Pediatrics (AAP) and The Australian Cancer Society of the potential need to occasionally apply these products to small areas of infant skin, DPDD recommended that these products be studied in infants younger than 6 months of age to obtain determine pharmacokinetic and safety data. Please refer to the March 3, 2006 review by DPDD.

## Review

The safety update derives from L'Oreal's Cosmetovigilance Database and from the literature.

The L'Oreal Cosmetovigilance Database contains post-marketing adverse events that were spontaneously reported primarily by consumers residing in countries where the most significant volume of L'Oreal products is sold. This database contains the following information;

1. For all ages, the average incidence of adverse events associated with use of all ecamsule-containing products from 1993 (when the product was first introduced in sunscreens, moisturizers and cosmetics) through 2004, was 0.0054% per million units sold. For children ( $\leq 16$  years of age), the corresponding incidence was 0.0142%. Although the incidence of adverse events was higher in children than in adults, the overall incidence of adverse events was very low in children. The most common adverse events, regardless of age, were dermatological with erythema and dermatitis being the most frequently reported. Much less frequently reported were allergic (allergic local reactions and urticaria), eye (e.g. conjunctivitis and lacrimation disorder) and respiratory (rhinitis) adverse reactions.
2. In 2004, the incidence of adverse events was similar to the average incidence in the 11-year period, from 1993-2004. In 2004, the incidence of adverse events per million units sold was 0.00489% for all ages and 0.0105% for children. Again, the incidence of adverse events was higher in children than in adults, but the overall incidence of adverse events was still very low in children. As reported over the 11 year period, the adverse events reported in 2004 were predominately dermatological, with erythema and dermatitis, being the most frequently reported, regardless of age. Allergic and eye adverse reactions were also reported but considerably less frequently than in the dermatological body system. In both children and subjects of all ages, the incidence of eye irritation (conjunctivitis and lacrimation disorder) was higher in 2004 compared 1993 through 2003 but they were still very low (<4.5 reports per million units sold).

3. Incidence of adverse events by year per million units sold for all ecamsule-containing products has remained relatively stable for all subjects regardless of age (analysis starting in 1993 through 2004) as well as for children (analysis starting in 1995 through 2004).
4. No new positive patch test reactions to ecamsule were reported between 2003 and 2004. However, there were 4 subjects with positive patch test reactions to other sunscreens contained in ecamsule-containing products; three were to octocrylene.
5. Upon the Sponsor's retrospective analysis each year of adverse events reported to the cosmetovigilance database, they reported no serious adverse events for the year 2004.

The Sponsor stated that there was no additional information in the literature on adverse reactions to ecamsule since the reporting date in NDA 21-471 through January 20, 2006.

An updated AERS search by this reviewer yielded similar adverse events to those reported by the Sponsor in their safety update and no AERS mentions for children between 0-1 years of age.

Please refer to the literature review conducted by DPDD and summarized in our previous consult review dated March 3, 2006 for similar sunscreen products (NDAs 21-501 and 21-502). Briefly, the American Academy of Pediatrics (AAP)<sup>1</sup> states that the safety of sunscreen use in infants less than 6 months of age is controversial. Concerns cited include the possibility of different absorptive characteristics of skin in infants younger than 6 months and immaturity of biological systems that metabolize and excrete drugs. However, the AAP points out that the Australian Cancer Society, supported by the Australian College of Dermatologists, has concluded that there is no evidence to suggest that using sunscreen on small areas of a baby's skin is associated with any long-term effects. They recommend their use when physical protection, e.g. clothing, hats and shade, is not adequate<sup>2</sup>. The AAP urges that parents be informed of the importance of avoiding high-risk sun exposure. They further state that it may be reasonable to apply sunscreen to small areas of the infant's skin that is not adequately protected by clothing, such as the face and backs of the hands.

The updated version of the Australian Cancer Society's Position Statement on this issue<sup>3</sup> again reiterates that there is no evidence that using sunscreen in infants is harmful<sup>4</sup>. They recommend that infants, 0-12 months of age, be kept out of the sun as much as possible. They state: "If infants are kept out of the sun or are well protected from UV radiation by clothing, hats and shade, then sunscreen need only be used occasionally on very small areas of an infant's skin." Potential side effects of sunscreen use in infants that are mentioned in this position statement include minor skin irritation and allergic contact

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<sup>1</sup> American Academy of Pediatrics Committee on Environmental Health. Ultraviolet Light: A Hazard to Children. *Pediatrics* 1999;104(2):328-333.

<sup>2</sup> Australian Cancer Society. *Policy Statement: Babies and Sunscreen*. Sydney, Australia: Australian Cancer Society; 1998.

<sup>3</sup> Cancer Council Australia and The Australian College of Dermatologists. *Position Statement. Sun Protection and Infants (0-12 months)*. May 2005.

<sup>4</sup> Marks R. The Use of Sunscreens in the Prevention of Skin Cancer. *Cancer Forum* 1996;20:211-215.

dermatitis from preservatives or perfumes in the product. They mention that sunscreen milks or creams formulated for sensitive skin usually contain titanium dioxide or zinc oxide and are less likely to contain alcohol or fragrances that may irritate the skin. They recommend that use be stopped immediately in the event of occurrence of an unusual reaction.

### **Conclusions**

Based on the information provided to DPDD and the acknowledgement by the AAP and The Australian Cancer Society that a sunscreen product may need to be occasionally applied to small areas of skin of infants less than 6 months of age that cannot be protected by clothing, it is recommended that these products be available to this age group. However, while there is no evidence that sunscreens are harmful to infants under 6 months of age, there is no direct evidence that they are safe in this age group. Also, there is need to determine the extent of systemic absorption of these products in young infants, which may be increased given their high body surface area to body weight ratio. As such, clinical study with collection of pharmacokinetic and safety data is needed in this age group. The data obtained from these studies will be critical to practitioners and other health care professionals who are consulted by parents and caregivers regarding the use of sunscreen products in infants less than 6 months of age. It is important to remember that, as emphasized by both the AAP and The Australian Cancer Society, sunscreen products are secondary to the primary protective measures which are avoidance/minimization of sun exposure of young infants and use of non-chemical protective measures (e.g. clothing, hats, umbrellas and canopies).

### **Recommendations**

DPDD recommends clinical study of sunscreen products in infants less than 6 months of age to obtain pharmacokinetic and safety data. It is recommended that these products be studied in infants with healthy intact skin because skin conditions such as eczema, which is prevalent in young infants, may be exacerbated by application of sunscreen to affected areas and systemic absorption of the product may be increased. Furthermore, consideration should be given to providing additional precautions in OTC labeling of sunscreen products if they are approved for use in infants less than 6 months of age so that parents and caregivers understand the appropriate place of these products in protecting young infants from UV radiation.

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/s/

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Jean Temeck  
5/2/2006 09:35:40 AM  
MEDICAL OFFICER

Lisa Mathis  
5/19/2006 03:29:16 PM  
MEDICAL OFFICER  
Concur

**MEMORANDUM**

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

**CLINICAL INSPECTION SUMMARY**

**DATE:** April 27, 2006

**TO:** Elaine Abraham., Regulatory Project Manager  
Diva Shetty, M.D., Medical Officer  
Division of Generic Drug Products

**THROUGH:** Constance Lewin, M.D., M.P.H.  
Branch Chief,  
Good Clinical Practice Branch I (GCPB1, HFD-46)  
Division of Scientific Investigations (DSI)

**FROM:** Roy Blay, Ph.D.  
Reviewer, GCPB1, DSI, HFD-46

**SUBJECT:** Evaluation of a Clinical Inspection

**NDA:** 21-471

**APPLICANT:** L'Oreal USA Products Inc.

**DRUG:** Sunscreen Filter Combinations

**THERAPEUTIC CLASSIFICATION:** Standard

**INDICATION:** Prevention of sunburn

**CONSULTATION REQUEST DATE:** November 29, 2005

**DIVISION ACTION GOAL DATE:** April 28, 2006

**PDUFA DATE:** July 28, 2006

- a. 125 subjects were screened, 100 subjects were randomized, and 99 subjects completed the study. There were no deaths or SAEs reported. One subject experienced an adverse event of mild headache. One subject withdrew consent. An audit of sixteen subjects' records was conducted including review of source documents and CRFs.
- b. There were no limitations to the inspection.
- c. Significant inspectional findings were as follows: Inspection revealed that the clinical investigator did not follow the protocol in that, for 25 subjects, only one test article, instead of two, was applied. No significant data discrepancies were noted.
- d. The data appear acceptable in support of the relevant indication.

### **III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS**

The inspection of Dr. Shanahan revealed that, as described above, the clinical investigator did not adhere to the protocol. Overall, the data appear acceptable in support of the respective indication.

*{See appended electronic signature page}*

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Roy Blay, Ph.D.  
Reviewer, Good Clinical Practice Branch I, HFD-46  
Division of Scientific Investigations

CONCURRENCE:

*{See appended electronic signature page}*

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Constance Lewin, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Branch I, HFD-46  
Division of Scientific Investigations

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/s/

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Roy Blay  
4/27/2006 03:35:47 PM  
CSO

Constance Lewin  
4/27/2006 03:41:30 PM  
MEDICAL OFFICER

## 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 Jong 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  
\_\_\_\_\_  
Ph.D., Consultant, \_\_\_\_\_

**Background:** FDA has previously discussed the cream vs. lotion issue with L'Oreal for their sunscreen products submitted under NDAs 21-501, 21-502, and 21-471. L'Oreal has provided the requested data. This discussion was scheduled so that FDA could inform L'Oreal of their decision.

**Discussion:** FDA has determined that the L'Oreal sunscreen products are creams. In making its decision, FDA followed the flow chart in the article of the International Journal of Pharmaceutics 295 (2005) 101-112, which was provided to L'Oreal. This article represents the FDA's current thinking on topical drug classification. The path FDA followed in the flow chart (page 109) was:

- topical dosage form for dermatology
- liquid or semisolid? (semisolid)
- contains greater than 50% water? (yes, 52 %)
- colloidal dispersion or emulsion? (emulsion)
- cream

L'Oreal stated that their product is borderline liquid or semisolid. If semisolid is chosen at the first part of the flow chart, it is impossible to arrive at a lotion. Also L'Oreal said

that this article is not a regulatory guidance. They pointed out footnote (a) which discusses Newtonian or pseudoplastic flow behavior and stated that their product exhibits pseudoplastic behavior.

FDA stated that the sunscreens show plastic behavior based on the data submitted by L'Oreal, including a high yield value of shear rate vs. shear stress. The difference between pseudoplastic and plastic behavior is the high yield value. FDA referred L'Oreal to Chapter 23 of Remington's Pharmaceutical Science on rheology.

L'Oreal asked if Remington's is a regulatory reference. FDA responded that is a scientific reference.

L'Oreal questioned why there is not a guidance on this final formulation issue so that all sponsors follow the same rule. L'Oreal felt that their company is being singled out. They noted that this issue was discussed three years ago with an earlier NDA, but still there is no regulatory guidance. L'Oreal stated that the Orange Book data standards manual does not distinguish between these dosage forms. They believed the International Journal of Pharmaceutics article has no regulatory weight. In addition, topical products under the monograph do not follow this reference.

In response, FDA stated that the article represents current agency thinking on this issue. Monograph products are marketed based on different regulatory requirements than NDAs. FDA pointed out that L'Oreal can challenge our decision through dispute resolution.

L'Oreal stated that if the dosage form issue is significant to FDA, the Agency should go through USP or present it in a public forum. FDA believed that this article was presented at a national meeting.

L'Oreal again expressed a concern that they are being singled out. FDA reiterated that this is current agency thinking and a scientifically-based decision, which would be applied to every applicant.

FDA asked L'Oreal to amend their applications as soon as possible, preferably early next week. L'Oreal stated that they would have to look at the CMC section to determine what changes are necessary. They will notify FDA by email when the amendment can be expected.

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/s/

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

**CONSULTATION RESPONSE**  
**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT**  
**OFFICE OF DRUG SAFETY**  
**(WO: 22, Mailstop 4447)**

**DATE RECEIVED:** January 6, 2006  
**DATE OF DOCUMENT:**  
 May 12, 2005

**DESIRED COMPLETION DATE:**  
 January 31, 2006  
**PDUFA DATE:** March 12, 2006

**ODS CONSULT #'s:**  
 06-0017 and 06-0042

**TO:** Andrea Leonard Segal, MD, Acting Director  
 Division of Nonprescription Clinical Evaluation, HFD-560

**THROUGH:** Nora Roselle, PharmD., Acting Team Leader  
 Denise Toyer, Pharm D., Deputy Director  
 Carol Holquist, RPh, Director  
 Division of Medication Errors and Technical Support, HFD-420

**FROM:** Linda M. Wisniewski, RN, Safety Evaluator  
 Division of Medication Errors and Technical Support, HFD-420

**PRODUCT NAME:**

**Anthelios SPF 15 Sunscreen Lotion (NDA# : 21-501)**  
 (Avobenzone 2%, Ecamsule 3%, Octocrylene 10% Lotion)

**Anthelios SPF 15 Moisturizing Sunscreen Lotion (NDA#: 21-502)**  
 (Avobenzone 2%, Ecamsule 2%, Octocrylene 10% Lotion)

**Anthelios SPF 20 Sunscreen Lotion (NDA#: 21-471)**  
 (Avobenzone 2%, Ecamsule 2%, Octocrylene 10%, and Titanium Dioxide 2%)

**NDA SPONSOR: L'Oreal USA Products**

**RECOMMENDATIONS:**

1. DMETS does not recommend use of the proposed proprietary name, Anthelios.
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. Because DDMAC does not have regulatory authority to review proposed OTC proprietary names, they did not comment on the name Anthelios.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.

**Division of Medication Errors and Technical Support (DMETS)  
Office of Drug Safety  
WO: 22; Mailstop: 4447  
Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** January 23, 2006

**NDA#s:** 21-501, 21-502, & 21-471

**NAME OF DRUG:** Anthelios SPF 15 Sunscreen Lotion (NDA# : 21-501)  
(Avobenzone 2%, Ecamsule 3%, Octocrylene 10% Lotion)

Anthelios SPF 15 Moisturizing Sunscreen Lotion (NDA#: 21-502)  
(Avobenzone 2%, Ecamsule 2%, Octocrylene 10% Lotion)

Anthelios SPF 20 Sunscreen Lotion (NDA#: 21-471)  
(Avobenzone 2%, Ecamsule 2%, Octocrylene 10%, and Titanium Dioxide 2%)

**NDA HOLDER:** L'Oreal USA Products

**\*\*\*NOTE:** This review contains proprietary and confidential information that should not be released to the public.\*\*\*

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Nonprescription Clinical Evaluation (HFD-560) for a review of the proprietary name, "Anthelios", regarding potential name confusion with other proprietary and/or established drug names. Container labels, carton and insert labeling were provided for review and comment.

**PRODUCT INFORMATION**

Anthelios is an over-the-counter sunscreen product that is currently marketed in Europe. It contains three active ingredients that include ecamsule, avobenzone, and octocrylene. Anthelios is for external use only. Three different formulations of Anthelios have been submitted for review.

Anthelios SPF 15 Moisturizing Sunscreen Lotion is a formulation that contains avobenzone (2%), ecamsule (2%), and octocrylene (10%) and will be supplied in 100 mL tubes. Anthelios Moisturizing Sunscreen Lotion is indicated for the prevention of sunburn and is to be applied evenly to cleansed skin before sun exposure and as needed.

Anthelios SPF 15 Sunscreen Lotion is a water resistant formulation that contains avobenzone (2%), ecamsule (3%), and octocrylene (10%) and will be supplied in 100 mL tubes. Anthelios Sunscreen Lotion is indicated for the prevention of sunburn and is to be applied liberally 15 minutes before sun exposure and reapplied as needed or after towel drying, swimming, or perspiring.

Anthelios SPF 20 Sunscreen Lotion is a water resistant formulation that contains avobenzone (2%), ecamsule (2%), octocrylene (10%), and titanium dioxide (2%) and will be supplied in 100 mL tubes. Anthelios SPF 20 Sunscreen Lotion is indicated in the prevention of sunburn and is to be applied liberally 15 minutes before sun exposure and reapplied as needed or after towel drying, swimming, or perspiring.

### III. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3</sup> for existing drug names which sound-alike or look-alike to Anthelios to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>4</sup>. The Saegis<sup>5</sup> Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

#### A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Anthelios. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Because DDMAC does not have regulatory authority to review proposed OTC proprietary names, they did not comment on the name Anthelios.
2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Anthelios. These products are listed in table 1 (see page 4), along with the dosage forms available and usual dosage.

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<sup>1</sup> MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> AMF Decision Support System [DSS], [Drugs@FDA](mailto:Drugs@FDA), the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

<sup>4</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

<sup>5</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel.

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Anthelios Sunscreen Lotion	Avobenzone/Ecamsule/Octocrylene Lotion 2%/3%/10%	Apply liberally 15 minutes before sun exposure and reapply as needed or after towel drying, swimming, or perspiring	NA
Anthelios SPF 15 Moisturizing Sunscreen Lotion	Avobenzone/Ecamsule/Octocrylene Lotion: 2%/2%/10%	Apply evenly to cleansed skin before sun exposure and as needed.	NA
Anthelios SPF 20 Sunscreen Lotion	Avobenzone/Ecamsule/Octocrylene/Titanium Dioxide Lotion: 2%/2%/10%/2%	Apply liberally 15 minutes before sun exposure and reapply as needed or after towel drying, swimming, or perspiring.	NA
Anthralin	Anthralin Cream, 1%	Apply once a day or as directed.	LA
			LA/SA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike) ***NOT FOI releasable.			

**B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)**

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Anthelios were discussed by the Expert Panel.

**C. PRESCRIPTION ANALYSIS STUDIES**

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Anthelios with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 125 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Anthelios (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 2   11913   Anthelios bottles	Order code: 11913 Anthelios 2 bottles
Inpatient RX: 2   11913   Anthelios bottles	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A for the complete listing of interpretation from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Anthelios, the primary concerns related to look-alike and/or sound-alike confusion with \_\_\_\_\_ and Anthralin.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Anthelios.

1. Look-alike and Sound-Alike Concerns

- a. \_\_\_\_\_ may look and sound similar to Anthelios. \_\_\_\_\_ is indicated in the \_\_\_\_\_ (\_\_\_\_\_ and older). \_\_\_\_\_ was the subject of ODS Consult \_\_\_\_\_, dated \_\_\_\_\_. The name \_\_\_\_\_ as found to be unacceptable at that time due to the potential for look-alike confusion with Anthralin.

NOTE: This review contains proprietary and confidential information that should not be released to the public.

Therefore, DMETS believes that there is significant potential for confusion involving both the over-the-counter and prescription products that may lead to error.

*Anthelios*

- b. Anthralin may look similar to Anthelios when scripted. Anthralin is indicated for the topical treatment of psoriasis. Both names contain nine letters and begin with the same four letters (Anth). The rest of the name may look similar due to similar placements of the upstrokes for the letter 'l'. There are also some overlapping product characteristics that may increase the potential for confusion further. Both products are topically administered, supplied in only one strength, and may be written to 'use as directed', as this is not an uncommon method of prescribing topically administered products. It is unlikely that a practitioner would write an order for an over-the-counter sunscreen product. However, practitioners could potentially write a prescription for "Anthralin UD, dispense #1" which could be misinterpreted for "Anthelios UD, dispense #1". This may be misinterpreted as a reminder for the patient and result in the patient being misdirected to the over-the-counter sunscreen area, and as a result the patient would receive the wrong product. The orthographic similarities, overlapping product characteristics, and the potential for similar prescribing practices increase the potential for confusion involving Anthelios and Anthralin.

*Anthelios*      *Anthralin*  
UD                      UD  
#1                        #1

## 2. Differentiation of Anthelios products that Contain Different Active Ingredients

Although DMETS does not recommend use of the proprietary name, Anthelios, we note that the sponsor proposes to market three products containing three different sets of active ingredients (avobenzone, ecamsule, octocrylene vs. two versions of avobenzone, ecamsule, octocrylene, titanium dioxide) with the same proprietary name. This is concerning because consumers would not know by the name alone that there are different active ingredients in each. If a consumer is allergic to a specific ingredient they may not realize that the active ingredients of the product may be different depending upon the SPF they choose. However, DMETS recognizes that the current practice, of naming OTC sunscreens, is to use the same proprietary name and distinguish them by using descriptors and/or the SPF number. Although DMETS does not recommend the use of the same proprietary name for products that contain different active ingredients for prescription products, we acknowledge that there is precedent for this naming convention with sunscreens in the Division of Nonprescription Clinical Evaluation. We also note that the sponsor prominently displays the SPF rating on the Principal Display Panel of each label thereby adequately differentiating each formulation.

### III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

For label and labeling comments, we refer you to ODS Consult # 06-0110 for Capital Soleil. The comments included in the review of Capital Soleil are applicable to Anthelios.

Appendix A:

ODS Consult: 06-0017 Anthelios

<b>Inpatient Written</b>	<b>Outpatient Written</b>	<b>Verbal</b>
Anthelias	Anthelios	Amphelius
Anthelias	Anthelios	Amphilia
Anthelio	Anthelios	Ampilios
Antheliol	Anthelios	Anthealos
Anthelios	Anthelios	Anthelias
Anthelios	Anthelios	antheliase
Anthelios	Anthelios	Anthelios
Anthelios	Anthelios	anthelios
Anthelios	Anthelios	Anthelios
Anthelios	Anthelios	Anthelious
Anthelios	Anthelios	Anthelius
Anthelios	Anthelios	Anthiliose
Anthelios	Anthelios	anthilius
Anthelios	Anthelios	
Anthelios		
anthelios		
Anthelios		
Authelios		

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/s/

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Linda Wisniewski  
3/9/2006 10:43:05 AM  
DRUG SAFETY OFFICE REVIEWER

Nora L. Roselle  
3/9/2006 10:56:05 AM  
DRUG SAFETY OFFICE REVIEWER

Denise Toyer  
3/9/2006 11:00:24 AM  
DRUG SAFETY OFFICE REVIEWER

Carol Holquist  
3/9/2006 12:39:54 PM  
DRUG SAFETY OFFICE REVIEWER

**CONSULTATION RESPONSE**  
**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT**  
**OFFICE OF DRUG SAFETY**  
**(WO22; Mail Stop 4447)**

<b>DATE RECEIVED:</b> January 6, 2006 <b>DATE OF DOCUMENT:</b> May 16, 2005	<b>DESIRED COMPLETION DATE:</b> January 31, 2006 <b>PDUFA DATE:</b> March 12, 2006	<b>ODS CONSULT #:</b> 06-0012 06-0043
<b>TO:</b> Andrea Leonard-Segal, M.D., Acting Director Division of Nonprescription Clinical Evaluation, HFD-560  <b>THROUGH:</b> Alina Mahmud, RPh, MS, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Errors and Technical Support, HFD-420  <b>FROM:</b> Felicia Duffy, RN, Safety Evaluator Division of Medication Errors and Technical Support, HFD-420		
<b>PRODUCT NAME:</b> <b>UV Expert (NDA 21-501)</b> (Avobenzone 2%, Ecamsule 3%, Octocrylene 10% Lotion)  <b>UV Expert (NDA 21-502)</b> (Avobenzone 2%, Ecamsule 2%, Octocrylene 10% Lotion)  <b>UV Expert (NDA 21-471)</b> (Avobenzone 2%, Ecamsule 2%, Octocrylene 10%, Titanium Dioxide 2% Lotion)		<b>NDA SPONSOR:</b> L'Oreal USA Products  <b>DISTRIBUTOR:</b> Lancôme

**RECOMMENDATIONS:**

1. Although we have not identified any proprietary or established names that would render the name "UV Expert" objectionable from a look-alike or sound-alike perspective, DMETS is concerned with the use of "Expert" in the name. We believe "Expert" is promotional and question what it communicates to consumers (see section III A of this review). For these reasons, DMETS does not recommend the use of the proprietary name UV Expert. However, if UV Expert is approved, we recommend relocating the SPF rating to appear immediately following the statement of identity in order to increase the prominence and clearly differentiate the current SPF 15 and SPF 20 formulations from future formulations (e.g., UV Expert Daily Face Protection Moisturizing Lotion SPF 15).
2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
3. Because DDMAC does not have regulatory authority to review proposed OTC proprietary names, they did not comment on the name UV Expert.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)  
Office of Drug Safety  
WO22; Mail Stop 4447  
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

**DATE OF REVIEW:** January 18, 2006

**NDA#s:** 21-501, 21-502, 21-471

**NAME OF DRUG:** **UV Expert 15 (NDA 21-501)**  
(Avobenzone 2%, Ecamsule 3%, Octocrylene 10% Lotion)

**UV Expert 15 (NDA 21-202)**  
(Avobenzone 2%, Ecamsule 2%, Octocrylene 10% Lotion)

**UV Expert 20 (NDA 21-471)**  
(Avobenzone 2%, Ecamsule 3%, Octocrylene 10%, Titanium Dioxide 2% Lotion)

**NDA HOLDER:** L'Oreal USA Products

**DISTRIBUTOR:** Lancôme

**I. INTRODUCTION:**

This consult was written in response to a request from the Division of Nonprescription Clinical Evaluation (HFD-560) for a review of the proprietary name, "UV Expert", regarding potential name confusion with other proprietary and/or established drug names. Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

The UV Expert products are over-the-counter (OTC) products that contain three or four ultraviolet radiation (UVR) filters providing protection throughout the ultraviolet B (UVB) and ultraviolet A (UVA) spectrum. The active ingredients include ecamsule, avobenzone, octocrylene, and/or titanium dioxide in the same or different concentrations. UV Expert is indicated for the prevention of sunburn will be available in a regular formulation and in a water resistant formulation. UV Expert is to be applied evenly to cleansed skin before sun exposure and as needed. The water resistant formulation is to be applied liberally 15 minutes before sun exposure and reapplied as needed or after towel drying, swimming or perspiring. A physician should be consulted for use in children under six months of age. UV Expert will be supplied in bottles containing 50 mL, and in tubes containing 100 mL.

**II. RISK ASSESSMENT:**

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3</sup> for existing drug names which sound-alike or look-alike to UV Expert to a degree where potential confusion between drug names could occur under

<sup>1</sup> MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> AMF Decision Support System [DSS], [Drugs@FDA](mailto:Drugs@FDA), the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted<sup>4</sup>. The Saegis<sup>5</sup> Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name UV Expert. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. Because over-the-counter drug products are regulated by the FTC, DDMAC is unable to provide comments on the proposed trade name UV Expert.
2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with UV Expert. This product is listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel.

Predict Name	Established name, Dosage form(s)	Usual adult dose	Other
UV Expert SPF 15	Avobenzone/Ecamsulf/Octocrylene Lotion: 2%, 2%, 10% and 2%, 3%, 10%	Apply to cleansed skin before sun exposure and as needed. Water resistant. Apply liberally 15 minutes before sun exposure and reapply as needed.	NA
UV Expert SPF 20	Avobenzone/Ecamsulf/Octocrylene/Titanium Dioxide Lotion: 2%, 2%, 10%, 2%	Apply liberally 15 minutes before sun exposure and reapply as needed.	
UV Expert SPF 15 Sunscreen Daily UVA/UVB Protection	No information available.	No information available.	
UV Expert DNA Shield SPF 50	No information available.	No information available.	LA/SA
UV Expert Extra Large Double Protection SPF 50	No information available.	No information available.	LA/SA

\*Frequently used, not all-inclusive. \*\*L/A (look-alike), S/A (sound-alike)

<sup>4</sup> WWW location <http://www.uspto.gov/tmdb/index.html>.

<sup>5</sup> Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com)

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to UV Expert were discussed by the Expert Panel.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of UV Expert with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 125 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two requisition prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for UV Expert (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Requisition #1: 	Order Code# 12 UV Expert 12 Bottles
Requisition #2: 	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for a complete listing of interpretations.

#### D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name UV Expert, the primary concerns related to look-alike and/or sound-alike confusion with UV Expert DNA Shield and UV Expert Extra Large Double Protection.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, UV Expert.

##### 1. Nomenclature Concerns with "Expert"

DMETS is concerned with the use of the modifier "Expert" in the proprietary name. We note the sponsor, Lancôme, uses this term with their sunscreen product line (e.g. UV Expert) and acknowledge there does not appear to be any safety concerns with the use of this modifier for this product. However, we question what "Expert" communicates to consumers and consider it promotional. DDMAC could not comment on the proprietary name UV Expert because they do not have regulatory authority to review proposed OTC proprietary names. The term "expert" has not been used in conjunction with any approved prescription drug product, and thus, this may establish precedence for other approved drug products. Although it is noted that there are no safety concerns with the use of the name "Expert" for these OTC products, DMETS notes that we would not recommend use of "Expert" for any prescription products because it is promotional. For these reasons, DMETS does not recommend the use of the proprietary name UV Expert.

##### 2. Look-alike and Sound-Alike Concerns

UV Expert is a sunscreen that will be distributed by Lancôme. While using the search engine [www.google.com](http://www.google.com), Lancôme UV Expert products (specifically, UV Expert DNA Shield SPF 50 and UV Expert Extra Large Double Protection SPF 50) were found for purchase on websites such as [www.amazon.com](http://www.amazon.com), [www.cosmeticamerica.com](http://www.cosmeticamerica.com) and [www.ebay.com](http://www.ebay.com). DMETS contacted Lancôme's consumer affairs via email to obtain information on the active ingredients in the Lancôme UV Expert products advertised on the aforementioned websites. The consumer affairs advisor indicated that "UV Expert has been discontinued and stock is no longer available. We have no way to obtain it for you to purchase." Thus, DMETS cannot review UV Expert DNA Shield SPF 50 and UV Expert Extra Large Double Protection SPF 50 due to lack of product availability and product information. DMETS has no objections to the proprietary name, UV Expert, from a look-alike, sound-alike standpoint. However, DMETS cautions the sponsor about the potential for consumers to confuse the discontinued Lancôme UV Expert products with the proposed Lancôme UV Expert products. For example, if a consumer previously purchased UV Expert SPF 15 Sunscreen Daily UVA/UVB Protection before it was discontinued, they may believe that the currently proposed UV Expert Sunscreen Daily Face Protection Moisturizer Lotion (SPF 15) is the same product. However, both products may have different active ingredients. It is possible that a consumer may have an allergic reaction to the proposed UV Expert product because they assumed it was the same as the discontinued product. Thus, we caution the sponsor to be aware of this potential issue.

### 3. Differentiation of UV Expert products that Contain Different Active Ingredients

We note that the sponsor proposes to market two products containing two different sets of active ingredients (avobenzone, ecamsule, octocrylene vs. avobenzone, ecamsule, octocrylene, titanium dioxide) and concentrations with the same proprietary name, UV Expert. This is concerning because consumers would not know by the name alone that there are different active ingredients in each. If a consumer is allergic to a specific ingredient they may not realize that the active ingredients of UV Expert may be different depending upon the SPF they choose. However, DMETS recognizes that the current practice, of naming OTC sunscreens, is to use the same proprietary name and distinguish them by using descriptors and/or the SPF number. Although DMETS does not recommend the use of the same proprietary name for products that contain different active ingredients for prescription products, we acknowledge that there is precedent for this naming convention with sunscreens in the Division of Nonprescription Clinical Evaluation. We note that the sponsor prominently displays the SPF rating on the principal display panel of each label. If the Division allows the use of the proprietary name UV Expert, DMETS recommends that the sponsor relocate the SPF rating on the principal display panel of the label to appear immediately following the statement of identity in order for the user to adequately differentiate this formulation from future formulations (e.g., UV Expert Sunscreen Daily Face Protection Moisturizer Lotion SPF 15).

### III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proprietary name UV Expert due to nomenclature concerns with the name "Expert".

- A. DMETS is concerned with the use of the modifier "Expert" in the proprietary name. We note the sponsor, Lancôme, uses this term with their sunscreen product line (e.g. UV Expert) and acknowledge there does not appear to be any safety concerns with the use of this modifier for this product. However, we question what "Expert" communicates to consumers and consider it promotional. DDMAC could not comment on the proprietary name UV Expert because they do not have regulatory authority to review proposed OTC proprietary names. The term "expert" has not been used in conjunction with any approved prescription drug product, and thus this may establish precedence for other approved drug products. Although it is noted that there are no safety concerns with the use of the name "Expert" for these OTC products, DMETS notes that we would not recommend use of "Expert" for any prescription products because it is promotional. For these reasons, DMETS does not recommend the use of the proprietary name UV Expert.

In the review of the container labels, carton and insert labeling of UV Expert, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

#### B. GENERAL COMMENT

1. Sun Protection Factor (SPF) is a recognized abbreviation on U.S. marketed sunscreens. However, the sponsor also uses PFA to indicate "Protection Factor UVA." DMETS questions whether this is a recognized term currently used and whether patients are aware of its meaning. If PFA is not recognized by users, then DMETS recommends deleting this term from the labels and labeling. If PFA is allowed, then the sponsor should use an asterisk (\*) on the principal display panel to refer user to the back panel where PFA is defined.
2. Relocate the SPF rating to appear immediately following the statement of identity (e.g., UV Expert Daily Face Protection Moisturizing Lotion SPF 15).

3. DMETS notes that the term 'Mexoryl™ SX' is a trademark for Ecamsule and the term 'ParsoI®' is a trademark for Avobenzone. Since the active ingredients, Ecamsule and Avobenzone, must be listed as part of the established name and active ingredients, delete all references to Mexoryl™ SX and ParsoI®, as they may be a source of confusion to patients who may think that this is a fourth or fifth active ingredient in the product.
4. Eliminate terminal zeros in the expression of strength and volume throughout labels and labeling. DMETS notes several incidents where a terminal zero is used in expression of the strength. The use of terminal zeros may result in error as often the decimals are overlooked. As evidenced by our post-marketing surveillance, the use of terminal zeros could potentially result in a ten-fold medication dose error. Although it is unlikely that a ten-fold dosing error would occur in this instance, the use of terminal zeros in the expression of strength or volume is not in accordance with the General Notice (page 10) of the 2004 USP, which states, '...to help minimize the possibility of error in the dispensing of administration of drugs...the quantity of active ingredients when expressed in whole numbers shall be shown without a decimal point that is followed by a terminal zero.' In addition, the use of terminal zeros is specially listed as a dangerous abbreviation, acronym, or symbol in the 2006 National patient Safety Goals of the Joint Commission of Accreditation of Healthcare Organizations (JCAHO). Lastly, safety groups such as ISMP also list terminal zeros on their dangerous abbreviations and dose designations list.
5. The proposed container label and carton labels for UV Expert (SPF 15) were provided in black and white, and may not represent the true color of the labels. Therefore, DMETS cannot assess if there are any safety concerns due to the colors utilized on the labels.

C. CONTAINER LABEL (Main Display Panel)

Include a statement of identity on the primary display panel to be in accordance with 21 CFR 201.61. 'The principal display panel of an over-the-counter drug in package form shall bear as one of its principal features a statement of the identity of the commodity. Such statement of identity shall be in terms of the established name of the drug, if any there be, followed by an accurate statement of the general pharmacological category (ies) of the drug or the principal-intended action (s) of the drug....The statement of identity shall be presented in bold face type on the principal display panel, shall be in a size reasonably related to the most prominent printed matter on such panel, and shall be in lines generally parallel to the base on which the package rests as it is designed to be displayed....'

APPEARS THIS WAY  
ON ORIGINAL