

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-812

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

Department of Health and Human Services
Food and Drug Administration

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

**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
21-812
NAME OF APPLICANT / NDA HOLDER
Pharmacia & Upjohn Co.
A Pfizer Company

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)
MEN'S ROGAINE EXTRA STRENGTH TOPICAL FOAM

ACTIVE INGREDIENT(S)
minoxidil

STRENGTH(S)
5%

DOSAGE FORM
Topical Foam

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

b. Issue Date of Patent

c. Expiration Date of Patent

d. Name of Patent Owner

Address (of Patent Owner)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

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.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? Yes No

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

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

2. Drug Substance (Active Ingredient)

- 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b)? Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

Appears This Way
On Original

- 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.)? 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.)? 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) 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.)

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

Bruce A. Pokras

1/12/2005

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.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Bruce A. Pokras	
Address 201 Tabor Road	City/State Morris Plains, NJ
ZIP Code 07950	Telephone Number (973) 385-5399
FAX Number (if available) (973) 385-7330	E-Mail Address (if available) bruce.a.pokras@pfizer.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.

Appears This Way
On Original

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/fdahtm/fdahtm.html>.

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 # 21-812

SUPPL #

HFD # 560

Trade Name Men's Rogaine Extra Strength

Generic Name 5% minoxidil topical aerosol

Applicant Name Pfizer Consumer Healthcare

Approval Date, If Known

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)(1)

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.

NA

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:

NA

d) Did the applicant request exclusivity?

YES NO

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

3 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?

NA

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).

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:

Investigaton #1: Study number 9140-006, A Double-Blind, Randomized, Placebo-Controlled Trial of the Efficacy and Safety of 5% Minoxidil Foam in the Treatment of Androgenic Alopecia in Males

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 <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input type="checkbox"/>

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

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

Investigation #1	YES <input type="checkbox"/>	NO <input checked="" type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input type="checkbox"/>

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"):

Investigaton #1: Study number 9140-006, A Double-Blind, Randomized, Placebo-Controlled Trial of the Efficacy and Safety of 5% Minoxidil Foam in the Treatment of Androgenic Alopecia in Males

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 # 50,063 YES ! NO
! Explain:

Appears This Way
On Original

Investigation #2
IND # YES ! NO
! Explain:

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

Investigation #1
!
! YES NO
! Explain: ! Explain:

Investigation #2
!
! YES NO
! Explain: ! Explain:

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

YES NO

If yes, explain:

Name of person completing form: Tia Frazier
Title: Regulatory Project Manager
Date: December 9, 2005

Name of Office/Division Director signing form: Andrea Leonard-Segal, M.D., M.S.
Title: Acting Division Director, Division of Nonprescription Clinical Evaluation, Office of Nonprescription Products

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

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

/s/

Andrea Segal

1/20/2006 01:13:42 PM

Appears This Way
On Original

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-812 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: March 24, 2005 Action Date: January 24, 2006

HFD 560 Trade and generic names/dosage form: Men's Rogaine Topical Aerosol

Applicant: Pfizer Consumer Healthcare Therapeutic Class: 4027510 (Hair Growth Products)

Indication(s) previously approved: NA

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

Number of indications for this application(s): 1

Indication #1: Androgenic alopecia of the vertex in men aged 18-49 years.

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

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived:

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

Reason(s) for partial waiver:

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

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ 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: _____

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

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ 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 21-812
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)

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

/s/

Tia Frazier
1/9/2006 02:10:36 PM

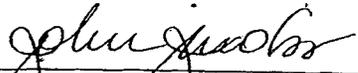
**Appears This Way
On Original**

1.3.3 Debarment Certification

1.3.3 DEBARMENT CERTIFICATION

CERTIFICATION UNDER SECTION 306(K)(1) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT (21 U.S.C. 335 a (k))

Pfizer Consumer Healthcare 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.



John R. Jacobs, Vice President
Global Regulatory Affairs

2/22/2005
Date

Appears This Way
On Original



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA NUMBER 21-812

Pfizer Consumer Healthcare
Pfizer Incorporated
Attention: Raymond Dann, Ph.D.
Regulatory Affairs Consultant
201 Tabor Road
Morris Plains, New Jersey.

Dear Dr. Dann:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Men's Rogaine (5% minoxidil) Topical Aerosol.

We also refer to the meeting between representatives of your firm and the FDA on January 17, 2006. The purpose of the meeting was to discuss two quality specifications for the product: 1) the evaluation of color as the product forms a solution and 2) the measurement of the pressure produced as the product is dispensed from its container.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Keith Olin, Regulatory Project Manager, at (301) 796-0962.

Sincerely,

{See appended electronic signature page}

Dr. John Smith, Ph.D.
Team Leader
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Appears This Way
On Original

Enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

MEMORANDUM OF TELECONFERENCE MEETING

MEETING DATE: January 17, 2006
TIME: 2:42-3:00PM
LOCATION: Teleconference
APPLICATION: NDA 21-812
DRUG NAME: Rogaine Topical Aerosol
TYPE OF MEETING: C (FDA requested meeting)

MEETING CHAIR: Dr. John Smith, Ph.D.

MEETING RECORDER: Tia Frazier, R.N., M.S.

FDA ATTENDEES:

Office of New Drug Quality Assessment

John Smith, Ph.D., Team Leader

Vispi Bhavnagri, Ph.D., Chemistry Reviewer

Office of Nonprescription Products

Division of Nonprescription Clinical Evaluation

Tia Frazier, R.N., M.S., Regulatory Project Manager

EXTERNAL CONSTITUENT ATTENDEES:

Regulatory Affairs

Raymond Dann, Ph.D., Regulatory Affairs Consultant

Global Regulatory Affairs-CMC

Susan Beavis, Director

BACKGROUND:

On March 23, 2005, Pfizer Consumer Healthcare submitted a new drug application (NDA) for Rogaine Topical Aerosol (5% minoxidil). FDA noted that the proposed color specification for the product in solution was a narrative description ~~_____~~, and was not precise. On December 8, 2005, FDA requested that Pfizer provide a more precise method of evaluation of the color of the solution. On December 22, 2005, Pfizer provided an interim response to FDA's request for a more precise measure of solution color, and committed to providing a full response by January 13, 2006.

On January 13, 2006, Pfizer submitted a response to FDA's December 8, 2005 request for a more accurate evaluation of the color of the solution inside the containers. On January 17, 2006,

FDA requested a meeting with Pfizer, and a teleconference meeting was arranged for the same day.

MEETING OBJECTIVES:

FDA requested this meeting to request more information about the proposed color specifications for the product in solution form, to request information about the pressure produced as the product is dispensed from its container.

DISCUSSION POINTS:

- Pfizer acknowledged that the color specification originally proposed as a release specification and stability indicator was not reliable, and allowed for too much variability.
- Pfizer proposed to incorporate the _____ as a replacement for the originally proposed narrative description specification. Specifically, Pfizer proposed that the release specifications require the foam at _____ to be clear and devoid of foreign matter, and be less than _____ described in the _____. Pfizer proposed that the stability specifications require the foam at _____ to be clear and devoid of foreign matter, and be less than _____ described in the _____.
 - FDA requested that Pfizer commit to a color specification of _____ for the foam at _____ as a stability specification.
 - FDA confirmed that Pfizer would need to submit a Prior Approval Supplement to change the labeled expiration date from _____ months if the product failed to meet the revised color specifications for stability.
- FDA also requested that Pfizer reexamine whether the pressure specifications could be tightened since the available stability data appear to support such a change.
- Pfizer agreed to consider tightening the pressure specifications after evaluating FDA's request internally.

ACTION ITEMS:

Pfizer would consider revising the color specification for stability at _____ to _____, and would contact FDA regarding its decision in a timely manner.

Pfizer will consider tightening the pressure specifications after evaluating the change internally. Pfizer will contact FDA when it has made a decision concerning this FDA request.

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

/s/

John Smith

1/20/2006 11:23:39 AM

Appears This Way
On Original



OTC Drug Labeling Review for Rogaine (5% Minoxidil) Topical Foam

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration
Rockville • MD 20857

SUBMISSION DATE(S):	March 23, 2005 May 11, 2005 January 18, 2006	RECEIVED DATE(S):	March 24, 2005 May 12, 2005 January 18, 2006
REVIEW DATE:	January 19, 2006		
NDA/SUBMISSION TYPE:	NDA 21-812		
SPONSOR:	Pfizer Consumer Healthcare		
DRUG PRODUCT:	Men's Rogaine Extra Strength Topical Foam		
ACTIVE INGREDIENT:	5% minoxidil		
PHARMACOLOGICAL CATEGORY:	Hair regrowth treatment		
STOCK KEEPING UNITS:	submitted labeling for carton (pillow pack), immediate container, and package insert for 60 g (2.11 fl oz) can (unscented)		
REVIEWER:	Matthew R. Holman, Ph.D.		

Appears This Way
On Original

BACKGROUND

On March 23, 2005, the sponsor submitted an NDA to market 5% minoxidil in a new dosage form, topical foam. On April 26, 2005, FDA contacted the sponsor to request annotated labeling to ensure that labeling meets requirements in 21 CFR 201.66(d). In response, the sponsor submitted N-000(BL) on May 11, 2005.

On January 9, 2006, FDA sent the sponsor a facsimile outlining necessary labeling revisions. In response, the sponsor sent revised labeling to FDA in an e-mail on January 18, 2006. On January 18, 2006, FDA notified the sponsor by telephone that the revised labeling was acceptable except for the first bulleted statement under *Other information*. FDA comments on January 9, 2006, incorrectly requested the following statement: “

However, in accordance with the January 5, 2006, labeling review, FDA should have requested the following statement: “hair growth has been shown in a clinical study of men (mostly white) aged 18-49 years who used it for 4 months.” The sponsor sent a facsimile to FDA on January 18, 2006, indicating that they would revise the statement as requested.

Appears This Way
On Original

3 Page(s) Withheld

 Trade Secret / Confidential

✓ Draft Labeling

 Deliberative Process

REVIEWER'S COMMENTS

The sponsor revised the labeling according to FDA's comments sent on January 9 and 18, 2006, except that the "Easy-to-use foam" statement remained on the PDP. To justify including this statement on the PDP, the sponsor submitted results from an actual use study. The study results reveal that nearly all study participants felt that this statement is accurate. Therefore, the statement is acceptable as proposed.

RECOMMENDATIONS

1. Issue an approval letter for Rogaine 5% minoxidil topical aerosol based on the submitted draft labeling and request final printed labeling.
2. Inform the sponsor that the "New" flag must be removed from labeling after six months.

**Appears This Way
On Original**

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

/s/

Matthew Holman
1/19/2006 01:47:51 PM
INTERDISCIPLINARY

Appears This Way
On Original



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA NUMBER 21-812

Pfizer Consumer Healthcare
Pfizer Incorporated
Attention: Raymond Dann, Ph.D.
Regulatory Affairs Consultant
201 Tabor Road
Morris Plains, New Jersey

Dear Dr. Dann:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Men's Rogaine (5% minoxidil) Topical Aerosol.

We also refer to the meeting between representatives of your firm and the FDA on January 13, 2006. The purpose of the meeting was to discuss the studies submitted to support the safety of the product.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Keith Olin, Regulatory Project Manager, at (301) 796-0962.

Sincerely,

{See appended electronic signature page}

Dr. Stanka Kukich, M.D.
Acting Director
Division of Dermatologic and Dental Drug
Products
Office of Drug Evaluation XX
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF TELECONFERENCE MEETING

MEETING DATE: January 13, 2006
TIME: 10:35-10:55 AM
LOCATION: Teleconference
APPLICATION: NDA 21-812
DRUG NAME: Rogaine Topical Aerosol
TYPE OF MEETING: C (FDA requested meeting)

MEETING CHAIR: Dr. Stanka Kukich, M.D.

MEETING RECORDER: Tia Frazier, R.N., M.S.

FDA ATTENDEES:

Division of Dermatologic and Dental Drug Products
Markham C. Luke, M.D., Medical Team Leader
Stanka Kukich, M.D., Acting Director

Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
Tia Frazier, R.N., M.S., Regulatory Project Manager

EXTERNAL CONSTITUENT ATTENDEES:

Regulatory Affairs
Raymond Dann, Ph.D., Regulatory Affairs Consultant

Medical Affairs
Rita Wanser, Associate Director

Statistics and Data Management
Paul Zhang, Senior Manager

BACKGROUND:

On March 23, 2005, Pfizer Consumer Healthcare submitted a new drug application (NDA) for Rogaine Topical Aerosol (5% minoxidil). FDA noted the product's potential to cause irritation and sensitization with repeated during the course of the clinical safety review.

Pfizer submitted a Repeat Insult Patch Test as part of Protocol MINOB-9140-004 to support repeated use of the product under maximum use conditions. FDA reviewers noted that Pfizer had modified the methods it employed to measure the potential for this product to cause skin irritation or to sensitization prior to the study's completion.

FDA was also concerned about adverse event reports of rash observed during the pivotal trial MINOB-9140-006.

On January 13, 2006, FDA requested a teleconference with Pfizer to discuss the submitted data concerning the contact sensitization and irritation studies submitted in Pfizer's March 23, 2005 NDA. A teleconference meeting was arranged the same day.

MEETING OBJECTIVES:

FDA requested this meeting to ask questions about the clinical safety studies, specifically the Repeated Insult Patch Test, and the adverse event reports signaling the product's irritancy or potential to invoke a sensitization response.

DISCUSSION POINTS:

In response to FDA's concerns about Pfizer's decision to modify the methodology for the occluded challenge tests before the study's completion, Pfizer stated its own conclusion that the irritating alcohol vehicle, length of the study (48 hours), and test (patch) materials led to the study subjects' inability to tolerate the test product under occlusion. They confirmed they modified the patch test procedure in response to these findings while the study was ongoing.

- Pfizer confirmed they lacked study data to support their position that the conditions of the test, including the materials, duration and vehicle, had caused the observed irritation response rather than the product itself.
- Pfizer confirmed that the Principle Investigator for this study had made a considerable financial investment in Pfizer, however, stated that they were reassured by an independent evaluation of the data.

Pfizer confirmed that two subjects dropped out of the pivotal efficacy trial (MINOB-9140-006) due to skin irritation (rash).

- Pfizer reported they would provide a summary of these rash adverse events after the meeting.

**Appears This Way
On Original**

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

/s/

Stanka Kukich

1/18/2006 02:13:10 PM

Appears This Way
On Original

1/17/06 ~~MAA~~ - pending accepted labeling

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-812	Efficacy Supplement Type SE-	Supplement Number
Drug: Rogaine Topical Foam Aerosol		Applicant: Pfizer Consumer Healthcare
RPM: Tia Frazier	HFD-560	Phone # 301-796-0890
<p>Application Type: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed and/or corrected</p>	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): Not applicable	
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		Type 3 (new dosage form)
• Other (e.g., orphan, OTC)		OTC
❖ User Fee Goal Dates		January 24, 2006
❖ Special programs (indicate all that apply)		<input type="checkbox"/> None <input type="checkbox"/> Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2
❖ User Fee Information		
• User Fee		<input type="checkbox"/> Paid UF ID number: <u>4796</u>
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify) NA
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify) NA
Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

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

Pfizer Consumer Healthcare
Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000



Consumer Healthcare

January 13, 2006

Charles J. Ganley, M.D. Director
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products (HFD-560)
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: **NDA 21-812**
Men's Rogaine® Extra Strength (5% Minoxidil) Topical Foam

Subject: **AMENDMENT TO A PENDING APPLICATION**
Response to FDA Request for Quality Information

Dear Dr. Ganley,

Reference is made to pending original New Drug Application (NDA) 21-812 for Men's Rogaine® Extra Strength (5% Minoxidil) Topical Foam submitted by Pfizer Consumer Healthcare on March 23, 2005. Reference is also made to FDA's December 8, 2005 request for a more precise evaluation of solution color. Pursuant to the Agency's request, Pfizer submitted an interim response on December 22, 2005 with a commitment to provide a full response by January 13, 2006. In accordance with our commitment, this amendment to pending NDA 21-812 contains a full response on the solution color issue.

Pursuant to 21 CFR 314.60(c), Pfizer Consumer Healthcare certifies that a true Field Copy of this Quality Amendment to New Drug Application 21-812 has been submitted to FDA's New Jersey District Office (Parsippany, NJ).

The data and information contained in this submission constitute trade secrets and confidential commercial information (see 21 C.F.R. 20.61), and Pharmacia & Upjohn, A Pfizer Company, hereby claims the legal protections afforded such trade secret and confidential information under 5 U.S.C. 552(b), 21 U.S.C. 331(j), and 18 U.S.C. 1905. Further dissemination may only be made with the express written permission of Pfizer.

+

Please contact me at 973-385-2687 with any Quality-related questions or issues. Please note that Dina Russello (973-385-4909) remains responsible for all other aspects of this application.

Sincerely,



Susan Beavis
Director, Global Regulatory Affairs-CMC

Appears This Way
On Original

cc: Tia Frazier, Regulatory Project Manager (cover letter only)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Pharmacia & Upjohn, A Pfizer Company	DATE OF SUBMISSION 1/13/06
TELEPHONE NO. (Include Area Code) (973) 385-5532	FACSIMILE (FAX) Number (Include Area Code) (973) 385-4300
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Pfizer Inc 201 Tabor Road Morris Plains, NJ 07950	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) 5% Minoxidil Topical Foam	PROPRIETARY NAME (trade name) IF ANY Men's Rogaine Extra Strength	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 2,4-pyrimidinediamine-6-(1-piperidinyl)-3-oxide	CODE NAME (If any)	
DOSAGE FORM: Topical Aerosol	STRENGTHS: 5%	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Hair Regrowth Treatment		

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)		
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)		
REASON FOR SUBMISSION FDA information request		
PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC		
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)		

This application contains the following items: (Check all that apply)

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

CERTIFICATION

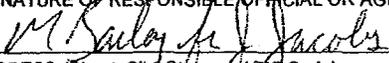
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA.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

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

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE John R. Jacobs, V.P. Global Regulatory Affairs	DATE: 1/13/06
ADDRESS (Street, City, State, and ZIP Code) 201 Tabor Road, Morris Plains, NJ 07950		Telephone Number (973) 385-5532

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

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

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.

Pfizer Response to FDA Request for a Precise Evaluation of Solution Color

(FDA question is presented in bold text followed by Pfizer's response)

Test procedure 73.5536 calls for observing the product at _____ when it forms a solution. The acceptance criteria for the color of that solution is vague _____, and is therefore inadequate as a control. Please provide for a more precise color evaluation (e.g., comparison with an appropriate reference standard).

Pfizer agrees that the description of _____ solution is subjective and we concur with the Agency that it would be preferable to utilize a more precise method for solution color evaluation. Therefore, in response to FDA's suggestion, Pfizer investigated the feasibility of developing a more objective method. After considering various options, Pfizer proposes that the solution description test be performed using _____ (see Attachment 1 for an overview of the instrument and see Attachment 2 for a copy of the methodology). Acceptance criteria are proposed based on data for samples with a color of greater than _____ and less than _____ that are still within limits for pH, assay, impurities (see Attachment 3 for a summary of results). Also note that the proposed acceptance criteria reflect yellowing of the solution on stability:

Solution Color Evaluation per Pfizer's 22 Dec 05 Amendment	Solution Color Evaluation per this Amendment
<p>Test: Description Test (Solution)</p> <p>Method: _____</p> <p>Acceptance Criteria: (for release and stability) At _____ the foam is a _____, with no visible foreign matter.</p>	<p>Test: Description Test (Solution)</p> <p>Method: _____</p> <p>Acceptance Criteria: (for release) At _____ the foam is a clear with no visible foreign matter and color is Not More Than _____</p> <p>(for stability) At _____ the foam is a clear with no visible foreign matter and color is Less Than _____</p>

In conjunction with our efforts to address FDA's comment related to the solution color at _____ Pfizer also took the opportunity to revisit the foam color at room temperature. As explained in the Pharmaceutical Development section of original NDA (items 3.2.P.2.2.5.1 and 3.2.P.2.2.5.2), the foam has been observed to become yellow on stability. Please note that this yellowing is considered a minor aesthetic issue. Based on the data in Attachment 3, Pfizer believes that the acceptance criteria for foam color on stability should be revised from _____ to "white to yellowish":

Foam Color Evaluation per Pfizer's 22 Dec 05 Amendment	Foam Color Evaluation per this Amendment
<p>Test: Description Test (Foam)</p> <p>Method: _____</p> <p>Acceptance Criteria: <i>(for release)</i> At room temperature, the foam is a white to off-white in color, creamy, and maintains structure during the one-minute observation period.</p> <p><i>(for stability)</i> At room temperature, the foam is a _____ _____ in color, creamy, and maintains structure during the one-minute observation period.</p>	<p>Test: Description Test (Foam)</p> <p>Method: _____</p> <p>Acceptance Criteria: <i>(for release)</i> At room temperature, the foam is a white to off-white in color, creamy, and maintains structure during the one-minute observation period.</p> <p><i>(for stability)</i> At room temperature, the foam is a white to yellowish in color, creamy, and maintains structure during the one-minute observation period.</p>

Appears This Way
On Original

6 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation OND

FACSIMILE TRANSMITTAL SHEET

DATE: January 9, 2006

To: Dina Russello	From: Tia Frazier
Company: Pfizer Consumer Healthcare	Division of Nonprescription Clinical Evaluation
Fax number: 973-385-4300	Fax number: (301) 796-9899
Phone number: 973-385-4909	Phone number: 301-796-0890
Subject: Required and Recommended Labeling Comments for your pending NDA 21-812 dated March 23, 2005	

Total no. of pages including cover: 3

Comments: These comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are subject to change as we finalize our review of your application. Additional labeling advice may be forthcoming.

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2080. Thank you.

Appears This Way
On Original

Labeling Comments

APPLICATION: NDA 21-812
DRUG NAME: Rogaine Topical Aerosol
SUBMISSION DATE: March 23, 2005

We request that you make the following revisions to the OTC labeling (outer and inner carton Principal Display Panels, outer and inner carton *Drug Facts* labeling, and consumer information leaflet):

Required Labeling Revisions for the Outer Carton and Inner Carton Principle Display Panels (PDPs):

1. Revise the dosage form name to read "topical aerosol" rather than "topical foam" in the statement of identity on the PDPs because "foam" is not a recognized dosage form name.
2. In accordance with 21 CFR 201.61(c), revise the statement of identity such that it appears in boldface type and in a size reasonably related to the most prominent printed matter on the PDPs.
3. Reduce the size of the word "FOAM" to match the font size of the statement of identity.
4. Remove the statement "extra strength." This statement may be added to the label only after you submit data that demonstrates that the topical foam aerosol is at least as effective as the 5% minoxidil solution.
5. Revise the statement "~~easy-to-use foam~~" to read "clinically proven to help regrow hair" to be consistent with the Rogaine topical solution labeling.
6. Remove the statement "easy-to-use foam" because it is not clear that this product is easy to use.

Required Outer Carton Labeling Revision:

1. Submit revised peel-back labeling that includes a prominent instruction to peel the label back for full drug labeling information. This instruction must be positioned outside the *Drug Facts* box on the outside of the peel-back label.

Required Labeling Revisions for the Outer Carton and Inner Carton Drug Facts Labeling:

2. Include instructions to wash hands after use under the *Directions* heading. Although this instruction appears in the consumer package insert, it should appear on all labeling.
3. Include the following statement as the first bulleted statement under the *Other information* heading: “hair growth has been shown in a clinical study of men (mostly white) aged 18-49 years” to be consistent with the Rogaine topical solution labeling.

Required Labeling Revisions for the Consumer Package Insert:

1. Revise the directions so that the text and illustration are consistent. The text instructs consumers to dispense the product in the palm of the hand. The illustration indicates that the product should be dispensed on the finger tips.

Recommended Labeling Revision for the Outer Carton Labeling (inside the fold-out flap):

1. You are encouraged to include the directions on how to dispense the right amount of the product with illustrations in the area on the inside of the fold-out flap. There appears to be sufficient labeling space to include the directions that appear in your consumer package insert in this section of the labeling.

**Appears This Way
On Original**

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

/s/

Tia Frazier
1/9/2006 12:52:27 PM
CSO

Appears This Way
On Original



Consumer Healthcare

sent to
Vispi John 12/22

December 22, 2005

Charles J. Ganley, M.D. Director
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products (HFD-560)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: **NDA 21-812**
Men's Rogaine® Extra Strength (5% Minoxidil) Topical Foam

Subject: **AMENDMENT TO A PENDING APPLICATION**
Response to FDA Request for Quality Information

Dear Dr. Ganley,

Reference is made to pending original New Drug Application (NDA) 21-812 for Men's Rogaine® Extra Strength (5% Minoxidil) Topical Foam submitted by Pfizer Consumer Healthcare on March 23, 2005. Reference is also made to FDA's December 8, 2005 request for Quality information (see attached email from Tia Frazier to Dina Russello). This amendment to pending NDA 21-812 contains:

- a *full response* to FDA's request for USP <381> data
- an *interim response* to FDA's request for a more precise evaluation of solution color, with a commitment to submit a full response by 13 January 2006

Pursuant to 21 CFR 314.60(c), Pfizer Consumer Healthcare certifies that a true Field Copy of this Quality Amendment to New Drug Application 21-812 has been submitted to FDA's New Jersey District Office (Parsippany, NJ).

This submission contains Confidential/Trade Secret information to which all claims of privilege and confidentiality are asserted in both statutory and common law. Further dissemination may only be made with the express written permission of Pfizer Inc.

Please contact me at 973-385-2687 with any Quality-related questions or issues. Please note that Dina Russello (973-385-4909) remains responsible for all other aspects of this application.

Sincerely,



Susan Beavis
Director, Global Regulatory Affairs-CMC

Appears This Way
On Original

cc: Tia Frazier, Regulatory Project Manager (cover letter only)

From: Frazier, Tia [mailto:FRAZIERT@cder.fda.gov]
Sent: Thursday, December 08, 2005 2:15 PM
To: Russello, Dina
Cc: Bailey, Michael; Ray.Dann@pfizer.com
Subject: Information Requests

Dear Ms. Russello,

We are reviewing the Chemistry, Manufacturing and Controls section of your March 23, 2005 NDA submission (NDA 21-812), and we have the following requests for information:

- USP General Chapter <601> (Aerosols, Metered-Dose Inhalers, and Dry Powder Inhalers) recommends that valve materials and other components that are in contact with an aerosol product meet the requirements under USP General Chapter <381> (Elastomeric Closures for Injections). Results from such testing were not found in this NDA. Please provide the indicated test data, either in an amendment to the NDA or, if this information can be found in a Drug Master File (DMF), via a specific DMF reference.
- Test procedure ~~calls for observing the product at~~, when it forms a solution. The acceptance criteria for the color of that solution is vague ~~and is therefore inadequate as a control~~. Please provide for a more precise color evaluation (e.g., comparison with an appropriate reference standard).

Please contact me if you have questions about these requests.

Tia Frazier, R.N., M.S.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Telephone: 301-796-0890
Fax: 301-796-9899
E-mail: fraziert@cder.fda.gov

10903 New Hampshire Ave.
Bldg #22, Room 5486
Silver Spring, MD 20993-0002

"MMS <secure.pfizer.com>" made the following annotations on 12/08/2005 02:15:41 PM

This message was sent in secure form from cder.fda.gov CDER Stamp

Appears This Way
On Original

Pfizer Response to FDA request for USP <381> data

(FDA question is presented in bold text followed by Pfizer's response)

USP General Chapter <601> (Aerosols, Metered-Dose Inhalers, and Dry Powder Inhalers) recommends that valve materials and other components that are in contact with an aerosol product meet the requirements under USP General Chapter <381> (Elastomeric Closures for Injections). Results from such testing were not found in this NDA. Please provide the indicated test data, either in an amendment to the NDA or, if this information can be found in a Drug Master File (DMF), via a specific DMF reference.

USP <381> testing was performed on both of the gaskets in the aerosol valve assembly. In particular, USP <381> testing was performed on the gasket associated with the mounting cup _____, and on the gasket associated with the valve stem _____ Results show that the gaskets produce extractables that are detected in water, product vehicle, and isopropanol:

USP <381> Testing	Target	Results	
		(lot 8148.09)	(lot 8148.10)
Heavy metals: Water Product vehicle*	NMT NMT	Meets Test LT LT	Meets Test LT LT
pH change: Water Product vehicle*	Report Results	Results Reported _____ _____	Results Reported _____ _____
Reducing agents: Water	Report Results	Results Reported _____	Results Reported _____
Total extractables: Water Product vehicle* Isopropanol	Report Results	Results Reported _____ _____ _____	Results Reported _____ _____ _____
Turbidity Water Product vehicle* Isopropanol	Report Results	Results Reported _____ _____ _____	Results Reported _____ _____ _____

* The Product Vehicle is composed of _____ USP (%w/w).

Abbreviations:
 NMT = not more than
 LT = less than
 ppm = parts per million
 NTU = Nephlos Turbidity Units

Please note that Pfizer does not consider the extractables detected by USP <381> testing to be relevant since there is no expectation that the components of the valve assembly will be exposed to _____ conditions during production or storage of the subject drug product. In contrast, Pfizer would agree that USP <381> testing of _____ is appropriate since such components are typically exposed to harsh _____ conditions during the production process for a parenteral product. Also note that USP <381> testing was conducted on _____ while the actual commercial package has only _____

To further support that the USP <381> results are inconsequential, Pfizer measured extractables from the entire container/closure system into product vehicle after storage for _____ No unexpected extractables were detected and an _____ of the residue was recorded to characterize the residue (see attached report dated 5/26/04 for complete details). Also, _____ and HPLC analyses were performed to confirm that specific extractables such as _____ are below detectable levels. Based on the totality of the information available, Pfizer believes there is adequate data to support that the proposed container closure system is suitable and compatible with the minoxidil foam product.

Appears This Way
On Original



MEMO

Date: 5/26/2004
To: R.L.Davison, W.J.Doskoczynski, M.J.Heintz, K.L.Lucas, A.McCormick,
J.A.Minerva, A.Petrillo, K.Warner, S.Wendling
From: D. Keiser, M.A. Smith, S.J. Borchert
Subject: Extracts from Minoxidil Foam Packaging
Substance Code: PNU-10858
cc: D.S.Aldrich, D.R.Myers, B.J.Pastore

Summary

Container/closure units for Minoxidil foam were filled with _____ and stored for _____ at _____ relative humidity (RH), both _____ and at _____ RH. The amount of extractable residue from container/closure units stored under both conditions was determined by weight as recommended earlier (1). Containers stored at _____ RH, _____ had _____ mg of residue from _____ units (_____ mg/unit); containers stored at _____ RH, _____ had _____ mg of residue from _____ units. _____ containers stored at _____ RH, _____ had a total of _____ mg of residue from _____ units.

Based on examination of the residue using _____, the residue is a mixture of _____ and a _____. These results are not unexpected since two of the _____ components are _____. In addition, _____
Based on these results it can be concluded that this container/closure system is compatible with Minoxidil foam.

Methods and Materials

The extractables from _____ container/closure units from lot UAAE stored _____ at _____ RH and from _____ container/closure units from the same lot stored _____ at _____

_____ were recorded using a _____
Parameters: Spectral resolution _____
Number of scans per spectrum _____
Spectral range _____
Detector _____

Discussion and Conclusions

The spectrum of the residue is presented in Figure 1. A search through reference libraries for a match produced the hit presented in Figure 2, a [redacted]. As seen in Figure 2, some peaks are not accounted for with this match. A search that focused on the peaks not represented by the [redacted] generated a hit with [redacted] (see Figure 3). Since two of the components ([redacted]) in the [redacted] are composed of [redacted] it is not surprising to find that [redacted] in the extracts. In addition, results for the USP <661> Physicochemical tests for both of these components were above the specification for the Nonvolatile Residue. This indicated that these [redacted] components could contribute significantly to extractables.

Subtracting the spectrum of [redacted] from the spectrum of the extracts, a difference spectrum is obtained that is presented in Figure 4. Searching the spectral libraries for a match produced the same hit as that presented in Figure 2. Figure 5 presents the difference spectrum and the [redacted]

[redacted] From the [redacted] spectrum alone it is difficult to further identify specific [redacted] which may be present.

Subtracting the spectrum for [redacted] from the difference spectrum presented in Figure 4 yields a featureless result, indicating that the bulk of the extractables is composed of an [redacted] and [redacted]. A comparison of the spectrum of the residue with the library spectrum of [redacted] demonstrated that the extracts did not contain a detectable level of this material. This is consistent with the findings of the HPLC study (3). Based on these results it can be concluded that this container/closure system is compatible with Minoxidil foam.

References

1. Keiser D, Borchert SJ, Davison RL, Heintz MJ. Compendial testing results of packaging components for Minoxidil foam. Pfizer memo to list. 26 May 2004.
2. Notebook Reference 35297DK67.
3. Pastore B. Validation of the Rogaine foam formulation for [redacted] extractable. Pfizer memo to list. To be issued.

Appears This Way
On Original

5 Page(s) Withheld

✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Pfizer Response to FDA Request for a Precise Evaluation of Solution Color

(FDA question is presented in bold text followed by Pfizer's response)

Test procedure _____ **calls for observing the product at** _____ **when it forms a solution. The acceptance criteria for the color of that solution is vague:** _____ **, and is therefore inadequate as a control. Please provide for a more precise color evaluation (e.g., comparison with an appropriate reference standard).**

Pfizer agrees that the description of _____ is quite subjective and we accept the Agency's suggestion to develop a more precise method for color evaluation. To that end, Pfizer has investigated the feasibility of using methodology in the European Pharmacopoeia (2.2.2 Degree of Coloration of Liquids). Unfortunately, the color standard range in the European Pharmacopoeia method 2.2.2 was found to be inadequate for our product. Therefore, Pfizer is currently exploring other options, including but not limited to a _____ that is sold by _____ (see attached information sheet). Please be assured that Pfizer is working to complete our method development effort as soon as possible and we anticipate being able to submit a final proposal to FDA no later than 13 January 2006.

Appears This Way
On Original

1 Page(s) Withheld

✓ Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Pharmacia & Upjohn, A Pfizer Company	DATE OF SUBMISSION 12/22/05
TELEPHONE NO. (Include Area Code) (973) 385-4909	FACSIMILE (FAX) Number (Include Area Code) (973) 385-4300
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Pfizer Inc 201 Tabor Road Morris Plains, NJ 07950	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Dina Russello, Director Global Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 21-812

ESTABLISHED NAME (e.g., Proper name, USP/USAN name) 5% Minoxidil Topical Foam	PROPRIETARY NAME (trade name) IF ANY Men's Rogaine Extra Strength
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 2,4-pyrimidinediamine-6-(1-piperidinyl)-3-oxide	CODE NAME (If any)
DOSAGE FORM: Topical Foam	STRENGTHS: 5%
PROPOSED INDICATION(S) FOR USE: Hair Regrowth Treatment	
ROUTE OF ADMINISTRATION: Topical	

APPLICATION DESCRIPTION

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

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE 505 (b)(1) 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
 Name of Drug _____ Holder of Approved Application _____

TYPE OF SUBMISSION (check one)
 ORIGINAL APPLICATION AMENDMENT TO PENDING APPLICATION RESUBMISSION
 PRESUBMISSION ANNUAL REPORT ESTABLISHMENT DESCRIPTION SUPPLEMENT EFFICACY SUPPLEMENT
 LABELING SUPPLEMENT CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT OTHER

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

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

REASON FOR SUBMISSION:
 FDA Request for Information - CMC

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

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

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

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

This application contains the following items: (Check all that apply)

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

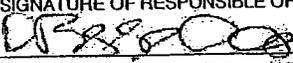
CERTIFICATION

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

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

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

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.
Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE Dina R. Russello, Director Regulatory Affairs	DATE: 12/22/05
ADDRESS (Street, City, State, and ZIP Code) 201 Tabor Road, Morris Plains, NJ 07950		Telephone Number (973) 385-4909

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

Department of Health and Human Services
 Food and Drug Administration
 WASHINGTON, DC 20204
 401 Rockville Pike
 Rockville, MD 20852-1448

Food and Drug Administration
 CDER (HFD-94)
 12229 Wilkins Avenue
 Rockville, MD 20852

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

Please contact me at the number below with any questions regarding this submission.

Sincerely,



Dina R. Russello
Director Regulatory Affairs
(973) 385-4909

Appears This Way
On Original

DUPLICATE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT Pharmacia & Upjohn, A Pfizer Company		DATE OF SUBMISSION 12/22/05	
TELEPHONE NO. (Include Area Code) (973) 385-4909		FACSIMILE (FAX) Number (Include Area Code) (973) 385-4300	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Pfizer Inc 201 Tabor Road Morris Plains, NJ 07950		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Dina Russello, Director Global Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950	

ORIGINAL AMENDMENT
N000 BL

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 21-812		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) 5% Minoxidil Topical Foam		PROPRIETARY NAME (trade name) IF ANY Men's Rogaine Extra Strength
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 2,4-pyrimidinediamine-6-(1-piperidinyl)-3-oxide		CODE NAME (If any)
DOSAGE FORM: Topical Foam	STRENGTHS: 5%	ROUTE OF ADMINISTRATION: Topical

PROPOSED INDICATION(S) FOR USE:

Regrowth Treatment

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)		
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)		
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)		
REASON FOR SUBMISSION FDA information request		
PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC		

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

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

This application contains the following items: (Check all that apply)

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

CERTIFICATION

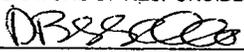
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA.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

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

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE Dina R. Russello, Director Regulatory Affairs	DATE: 12/22/05
ADDRESS (Street, City, State, and ZIP Code) 201 Tabor Road, Morris Plains, NJ 07950		Telephone Number (973) 385-4909

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

Department of Health and Human Services
and Drug Administration
HFD-99
Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

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



OTC Drug Labeling Review for Rogaine (5% Minoxidil) Topical Foam

Office of Nonprescription Products
Center for Drug Evaluation and Research • Food and Drug Administration
Rockville • MD 20857

SUBMISSION DATE(S):	March 23, 2005 May 11, 2005	RECEIVED DATE(S):	March 24, 2005 May 12, 2005
REVIEW DATE:			January 5, 2006
NDA/SUBMISSION TYPE:			NDA 21-812
SPONSOR:			Pfizer Consumer Healthcare
DRUG PRODUCT:			Men's Rogaine Extra Strength Topical Foam
ACTIVE INGREDIENT:			5% minoxidil
PHARMACOLOGICAL CATEGORY:			Hair regrowth treatment
STOCK KEEPING UNITS:			submitted labeling for carton (pillow pack), immediate container, and package insert for 60 g (2.11 fl oz) can (unscented)
REVIEWER:			Matthew R. Holman, Ph.D.

Appears This Way
On Original

BACKGROUND

On March 23, 2005, the sponsor submitted an NDA to market 5% minoxidil in a new dosage form, topical foam. The sponsor indicates that it would like to market unscented and scented products. The sponsor submitted labeling for the unscented product and indicates that labeling for the scented product will be identical except as relates to the fragrance.

On April 26, 2005, FDA contacted the sponsor to request annotated labeling to ensure that labeling meets requirements in 21 CFR 201.66(d). In response, the sponsor submitted N-000(BL) on May 11, 2005.

Appears This Way
On Original

4 Page(s) Withheld

 Trade Secret / Confidential

✓ Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative- 5

F. "Easy-to-use foam"

The sponsor must remove this statement because it is not clear that this product is easy to use.

II. Drug Facts Box

A. Format Specifications

The proposed format specifications, such as font, type size, or barline/hairline thickness, meet the requirements of 21 CFR 201.66 and, thus, are acceptable.

B. Peel-Back Label

The proposed label utilizes a peel-back label such that the Drug Facts box begins on the back of the pillow pack and continues as the label is peeled back. The proposed layout is acceptable as proposed except the sponsor must include a prominent instruction to peel-back label for more information.

C. *Active ingredient/Purpose*

The proposed labeling list the active ingredient as "5% w/w (without propellant)." The labeling is acceptable as proposed.

D. *Uses*

The labeling is acceptable as proposed.

E. *Warnings*

The proposed labeling is identical to NDA 20834/SCS-007 except for the flammability warning. In SCS-007, this warning reads as follows: "**Flammable:** keep away from fire or flame." The proposed warning in this NDA reads as follows: "**Extremely Flammable:** Avoid fire, flame, or smoking during and immediately following application." The proposed warning is acceptable because it instructs consumers to be even more cautious about flammability with the topical foam aerosol in comparison to the topical solution. This warning seems appropriate, as the foam contains flammable propellants that the topical solution lacks and it was tested for flammability according to 16 CFR 1500.45 and 1500.46.

F. *Directions*

The proposed directions instruct consumers to "apply half a capful 2 times a day" and refers consumers to the consumer package insert for more detailed instructions. The consumer package insert instructs consumers to hold cap in hand and spray foam on

fingers, estimating the amount of foam that is half a capful. The sponsor submit data from actual use studies demonstrating that subjects could somewhat accurately administer the correct dose of minoxidil (i.e., 1.0 gram). Although the results from this study reveal a significant amount of variability in minoxidil dispensed, the proposed directions are acceptable. The effectiveness study involved subjects applying minoxidil according to the proposed directions. Therefore, the product should be effective when used according to the proposed directions (even if dosing variabilities exists). However, the sponsor should include instructions to wash hands after use. Although this instruction appears in the consumer package insert, it should appear on all labeling.

G. Other information

The proposed labeling does not reference results of clinical studies, as done in NDA 20834/SCS-007. The proposed labeling includes a new statement regarding the can being pressurized. The submitted effectiveness study was conducted on male (mostly white) subjects under the age of 50 years. According to the clinical review, the effectiveness of the products on males under 50 years cannot be extrapolated to males 50 years and over. Therefore, the sponsor must include the following statement as the first bulleted statement under this heading: "hair growth has been shown in a clinical study of men (mostly white) aged 18-49 years who used it for 4 months."

H. Inactive Ingredients, Questions?

The labeling is acceptable as proposed.

III. Area outside of Drug Facts Box

1. The proposed labeling with scalp pictures includes the same pictures and information as appears on the labeling in NDA 20834/SCS-007. The proposed labeling is acceptable.
2. The sponsor should be encouraged to include the directions on how to dispense the right amount of the product with illustrations in the area on the inside of the fold-out flap. There appears to be sufficient labeling space to include the directions that appear in the consumer package insert.

Appears This Way
On Original

- name. In accordance with 21 CFR 201.61(c), revise the statement of identity such that it appears in boldface type.
2. The promotional statement "New" on the principal display panel is acceptable, but should be removed after six months.
 3. Remove the statement "extra strength." This statement may be added to the label only if the sponsor submits data demonstrating that the topical foam aerosol is at least as effective as the 5% minoxidil solution.
 4. Consistent with the Rogaine topical solution labeling, revise the statement ~~_____~~ to read "clinically proven to help regrow hair."
 5. Remove the statement "easy-to-use foam" because it is not clear that this product is easy to use.
 6. The proposed layout with a peel-back label is acceptable. However, include, outside the Drug Facts box on the outside of the peel-back label, a prominent instruction to peel-back label for more information.
 7. Include instructions to wash hands after use under the *Directions* heading. Although this instruction appears in the consumer package insert, it should appear on all labeling.
 8. Consistent with the Rogaine topical solution labeling, include the following statement as the first bulleted statement under the *Other information* heading: "hair growth has been shown in a clinical study of men (mostly white) aged 18-49 years who used it for 4 months."
 9. You are encouraged to include the directions on how to dispense the right amount of the product with illustrations in the area on the inside of the fold-out flap. There appears to be sufficient labeling space to include the directions that appear in the consumer package insert.
- II. Communicate the following comments regarding consumer package insert to the sponsor prior to the PDUFA goal date:
1. Revise the directions so that the text and illustration are consistent. The text instructs consumers to dispense the product in the palm of the hand. The illustration indicates that the product should be dispensed on the finger tips.

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

/s/

Matthew Holman
1/6/2006 08:45:27 AM
INTERDISCIPLINARY

Andrea Segal
1/6/2006 12:21:51 PM
MEDICAL OFFICER

Appears This Way
On Original

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

/s/

Tia Frazier
12/22/2005 01:22:31 PM
CSO

Appears This Way
On Original

Frazier, Tia

From: Frazier, Tia
Sent: Monday, December 19, 2005 3:53 PM
To: 'dina.russello@pfizer.com'
Subject: Information Request

Dear Ms. Russello,

Provide information to substantiate safety and efficacy and to forgo a possible restriction in labeling with regard to use of Rogaine Aerosol Foam, 5%, in patients age 50 years and older. This submission should include any data regarding the safety and efficacy of use in the geriatric population.

We request that you provide this information by the end of the business day on Wednesday, December 21, 2005.

Thank-you,

Tia Frazier

Appears This Way
On Original

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

/s/

Tia Frazier
12/19/2005 04:59:19 PM
CSO

**Appears This Way
On Original**

Frazier, Tia

From: Frazier, Tia
Sent: Thursday, December 08, 2005 2:15 PM
To: 'Dina Rusello (dina.russello@pfizer.com)'
Cc: 'michael.bailey@pfizer.com'; 'Ray.Dann@pfizer.com'
Subject: Information Requests

Dear Ms. Russello,

We are reviewing the Chemistry, Manufacturing and Controls section of your March 23, 2005 NDA submission (NDA 21-812), and we have the following requests for information:

- USP General Chapter <601> (Aerosols, Metered-Dose Inhalers, and Dry Powder Inhalers) recommends that valve materials and other components that are in contact with an aerosol product meet the requirements under USP General Chapter <381> (Elastomeric Closures for Injections). Results from such testing were not found in this NDA. Please provide the indicated test data, either in an amendment to the NDA or, if this information can be found in a Drug Master File (DMF), via a specific DMF reference.
- Test procedure _____ calls for observing the product at _____, when it forms a solution. The acceptance criteria for the color of that solution is vague (i.e., _____), and is therefore inadequate as a control. Please provide for a more precise color evaluation (e.g., comparison with an appropriate reference standard).

Please contact me if you have questions about these requests.

Tia Frazier, R.N., M.S.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Telephone: 301-796-0890
Fax: 301-796-9899
E-mail: fraziert@cder.fda.gov

10903 New Hampshire Ave.
Bldg #22, Room 5486
Silver Spring, MD 20993-0002

Appears This Way
On Original



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation OND

FACSIMILE TRANSMITTAL SHEET

DATE: November 28, 2005

To: Dina Russello	From: Tia Frazier
Company: Pfizer Consumer Healthcare	Division of Nonprescription Clinical Evaluation
Fax number: 973-385-4300	Fax number: 301-796-9899
Phone number: 973-385-4909	Phone number: 301-796-0890
Subject: Information Request	

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 796-2080. Thank you.

Appears This Way
On Original

Message: Please refer to your new drug application (NDA 21-812) dated March 23, 2005 for Men's Rogaine Extra Strength Topical Foam (5% minoxidil topical aerosol). We have the following urgent information request:

- Please provide the raw data on the amount of product dispensed by each subject included in the three Actual Use Studies submitted in the NDA described above.

Appears This Way
On Original

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

/s/

Andrea Segal
11/10/2005 10:47:04 AM

Appears This Way
On Original

3890

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Office/Division): Mary Jean Kozma-Fornaro
Division of Dermatologic and Dental Drug Products

FROM (Name, Office/Division, and Phone Number of Requestor): Tia Frazier
Division of Over-the-Counter Drug Products

DATE
4/21/05

IND NO.

NDA NO.
21-812

TYPE OF DOCUMENT
New Drug Application

DATE OF DOCUMENT
March 23, 2005

NAME OF DRUG
5% Minoxidil Topical Foam

PRIORITY CONSIDERATION
H

CLASSIFICATION OF DRUG
Type 3 (new dosage form)

DESIRED COMPLETION DATE
January 2, 2006

NAME OF FIRM: Pharmacia & Upjohn, A Pfizer Company

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|---|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input checked="" type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> .SSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: Please review and comment on the adequacy of the safety and efficacy data in the pivotal clinical safety and efficacy study MINOB-9140-006 and dermal sensitization study MINOB-9140-004 to support approval of a new 5% minoxidil foam formulation (NDA 21-812). Please comment on whether these studies support approval of this NDA from a clinical perspective.

SIGNATURE OF REQUESTOR
Tia Frazier, Regulatory Project Manager

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

STUDY ENDPOINT REVIEW

Table of Contents

1	EXECUTIVE SUMMARY & RECOMMENDATIONS.....	3
2	ENDPOINT REVIEW	4
2.1	CONSULT REQUEST	4
2.2	STUDY DESCRIPTION	4
2.3	ENDPOINT CONCEPT: CHANGE IN NUMBER OF NON-VELLUS HAIRS.....	5
2.3.1	Procedure for hair counts	5
2.3.2	Results.....	5
2.4	ENDPOINT CONCEPT: PATIENT EVALUATION OF HAIR GROWTH PATTERN	5
2.4.1	Description of Patient Assessment	5
2.4.2	Findings based on Patient Assessment	6
2.4.3	Comments on Patient Assessment	6
2.4.4	Conclusions Based on Patient Assessment	8
2.5	SECONDARY ENDPOINTS.....	8
2.5.1	Expert Panel Review of Photographic Evidence of Hair Growth	8
2.5.2	Percent Change in Hair Count.....	9
2.6	ENDPOINT CONCLUSIONS.....	9
3	APPENDICES:.....	11
3.1	NORWOOD HAMILTON SCALE FOR ANDROGENETIC ALOPECIA.....	11
3.2	SUBJECT QUESTIONNAIRE FROM PFIZER PROTOCOL MINOB-9140-006.....	12
4	REFERENCES.....	13

Appears This Way
On Original

STUDY ENDPOINT REVIEW

score that ranged from Significantly Worse (-3) to Significantly Improved (+3), with a midpoint anchor of No Change (0).

2.4.2 Findings based on Patient Assessment

Compared with the patients receiving placebo, approximately 30% more of the patients receiving minoxidil indicated that their hair loss pattern improved at least slightly from baseline to end of 16 weeks of treatment based on the patient self-assessment of photographs.

Table 2: Percent of Patients Reporting Each Level on the Patient Assessment of Change in Hair Loss

Subject assessment	PBO %	5% Difference (Minoxidil - PBO)	
-3 Significantly Worse	0.00%	0.00%	0.00%
-2 Moderately Worse	4.70%	0.61%	-4.08%
-1 Slightly Worse	14.77%	5.52%	-9.24%
0 No change	35.57%	17.79%	-17.78%
1 Slightly Improved	22.82%	23.93%	1.11%
2 Moderately Improved	16.11%	27.61%	11.50%
3 Significantly Improved	5.37%	23.31%	17.94%
Missing	0.67%	1.23%	0.56%

Correlation of the patient's perception and the hair counts are reported in Table 3.

Table 3: Correlation of Patient Report with Computerized Non-Vellus Hair Counts

	Placebo		5% Minoxidil		Overall	
Pearson Correlation (p-value)	0.085	(0.303)	0.136	(0.084)	0.228	< 0.001
Spearman Correlation (p-value)	0.078	(0.343)	0.142	(0.073)	0.224	< 0.001

Statistically significant differences in mean change from baseline to week 16 were observed in this study. The mean change in hair growth pattern was 1.4 points for patients receiving 5% minoxidil versus 0.5 points for patients treated with placebo ($p < 0.0001$).

For subjects who indicated that their hair loss pattern had improved (scores of +1, +2, or +3 based on review of Polaroid photographs), the average hair count increased by 11.3 hairs/cm² in patients receiving placebo and by 17 hairs/cm² in the patients treated with minoxidil.

2.4.3 Comments on Patient Assessment

1. In this study, patients provided an evaluation of the amount of hair growth change they observed based on review of photographs. It is not clear that the measure used in this study is adequate to the task of documenting the patients' perceived change in hair

STUDY ENDPOINT REVIEW

growth. There are several factors that may have undermined the reliability and validity of this endpoint measure that must be considered in the review of this NDA submission.

- a. Evidence that patients comprehended the assessment task was not provided
 - i. Technical terms (i.e., “the vertex region of your head”) are informative to trained clinicians but patients may not have understood what they were supposed to evaluate
 - ii. The question posed in the patient self-assessment is complex and may be difficult for patients with low literacy levels to follow.
 - iii. Endpoints measured using patient self-report need to be collected in a language the patient can speak and read fluently. If translations are required for non-native English speakers participating in trial, the translations need to be conducted and validated to ensure that they produce valid and comparable data to those in the original language version. This comparability must be demonstrated before pooling questionnaire data from different language versions for statistical analysis.

The eligibility requirements for this trial did not require all patients to be native English speakers or fluent in English as spoken in the USA. If non-native English speakers were included in the study population, were adequate translations of these questions provided to ensure comparable instructions and question wording? It was not clear that all patients in the study were native or fluent English speakers. This should be confirmed. If all were not fluent in English as spoken in the USA, how was translation of this question handled? Was an adequately developed translation provided for non-native/non-fluent English speakers to complete? If so it should be documented and submitted to the NDA. Were translations performed by study personnel on an as needed basis? What testing was conducted to ensure that ad hoc translations were adequate?

- b. Instructions for the patient assessment did not make clear that responses were to be based solely on comparisons of the baseline and Week 16 Polaroid photographs. The instructions did not preclude the patient from considering other information in his evaluation.
 - i. If hair growth patterns involved an increase in marginally non-vellus hairs, the patient may feel the presence of new hair growth that is not visible on the photographs and use that information to inform his response. In so doing, he is not actually performing the task indicated in the assessment because he is considering additional information to that evaluated by the expert panel.

STUDY ENDPOINT REVIEW

- ii. If a patient experienced contact dermatitis (scalp irritation, dryness, itching, scaling, and redness), both the patient and his clinician may no longer be blinded to treatment.
2. The patient assessment of improvement in hair loss was weakly correlated with the change in hair counts. This may have been due, at least in part, to the poorer quality of the photographs patients were given to review. Adequate photographs are critical for providing information for patient review. While a clinician can examine the patient's head in detail and enjoys the benefit of comparisons with the heads of many patients, the patient has limited ability to see his own scalp or to assess changes in the perimeters of the scalp area. If lighting was not well controlled, if the angle or distance of the camera relative to the vertex was not adequately standardized, the evidence the patients reviewed may not have been adequate to provide a valid assessment of changes in hair growth pattern.
3. The patient and clinician evaluation of change in hair growth evident in Polaroid photographs also were poorly correlated. Review of the data listings suggests much of which was due to "no change" scores reported by the clinicians for patients who reported "moderate" or "significant" improvement. While there were a number of patients in the placebo group who responded, the data raise questions about what else patients were considering (in addition to the Polaroid photos) to evaluate their treatments. (see 1.b above for two possible explanations).

2.4.4 Conclusions Based on Patient Assessment

1. We are concerned that the patient reported perceived hair growth assessment may not be based on an adequately blinded and validated assessment.
2. The patient assessment may include perceptions of vellus or miniaturized non-vellus hair growth that are not relevant for evaluation of non-vellus hair growth.

2.5 Secondary Endpoints

2.5.1 Expert Panel Review of Photographic Evidence of Hair Growth

A secondary endpoint for this trial was based on the mean of scores from three clinicians who served as an expert panel. Each expert reviewed the same Polaroid photographs the patients reviewed then used the same scale that the patients used to evaluate change in hair growth patterns.

Results for the endpoint based on the median score from expert panel evaluation of photographs are statistically significant but suggest a very small benefit associated with minoxidil. The median EPR score for minoxidil treated patients was 0.5 while that for the placebo treated patients was 0. This is likely due to the fact that clinician reports (particularly those of Dr. _____) were more likely to indicate "no change" than was true for patient-self-assessments in either the placebo or minoxidil treated patients.

STUDY ENDPOINT REVIEW

Kappa statistics for correspondence of the median expert panel score with the patient scores were low (range 0.03 to 0.13), which indicates relatively low association between assessments by clinicians and patients based on the same photographs. Kappas for agreement among the experts were higher (range 0.15 to 0.48). [I question the appropriateness of Kappa for ordinal data with 7 possible levels, as it assumes no correspondence if scores are not identical, and depends on how ties are handled.] At least two possible explanations for differences between the patient and the clinician include the possibility that patients considered additional information beyond what was included in the photographs (e.g., sensation of vellus and miniaturized non-vellus hair growth; experience of hair loss associated with minoxidil treatment.)

2.5.2 Percent Change in Hair Count

Statistically significant, but small changes were observed in % change in hair counts (as shown in table 4 below).

Table 4: Percent (%) change in hairs/cm² from baseline to Weeks 8, 12, and 16 assessments (ITT population)

	Placebo	5% Minoxidil	
	Percent Change in hairs/cm ²		(p-value)
Baseline to Week 8	3.4	10.4	<0.0001
Baseline to Week 12	3.3	13.0	<0.0001
Baseline to Week 16	3.3	13.7	<0.0001

If the difference observed in the placebo group is factored out of the minoxidil effects, the percent change in the hair counts is less than 10% at week 8 and week 12, and only slightly greater than 10% at week 16.

2.6 Endpoint Conclusions

1. There was little association between hair counts and patient or clinician perceived change in hair growth patterns. Whatever the source of variability in these different endpoints, the results suggest only a subset of patients experienced a noticeable improvement, and those improvements tended to be modest improvement with 16 weeks of twice daily 5% minoxidil therapy.
2. The data based on the patient assessment may not be valid because the question they were asked to answer to evaluate hair loss patterns may not have been adequately understood by all patients. It also may not have been worded in a way that makes clear that the patients were supposed to consider only the photographs to evaluate the change in their hair growth.

STUDY ENDPOINT REVIEW

3. If the patient experienced contact dermatitis (scalp irritation, dryness, itching, scaling, and redness) he and his clinician may no longer be blinded to the treatment received. This raises significant concerns about reliance on findings from the patient assessments to evaluate the efficacy of this treatment.
4. Weak association between patient and clinician panel evaluation of change in the hair growth patterns based on the same photographs reflect the tendency for clinician review of the same photographs to be evaluated as showing no change. Due to the other questions raised in the review of the patient assessment, the poor correspondence between clinician assessment and hair counts indicates very limited clinical benefit can be expected from this therapy.
5. Any description of the results based on this study should reflect the poor correspondence between "perceived" and measured hair growth.

Appears This Way
On Original

3 APPENDICES:

3.1 Norwood Hamilton Scale for Androgenetic Alopecia

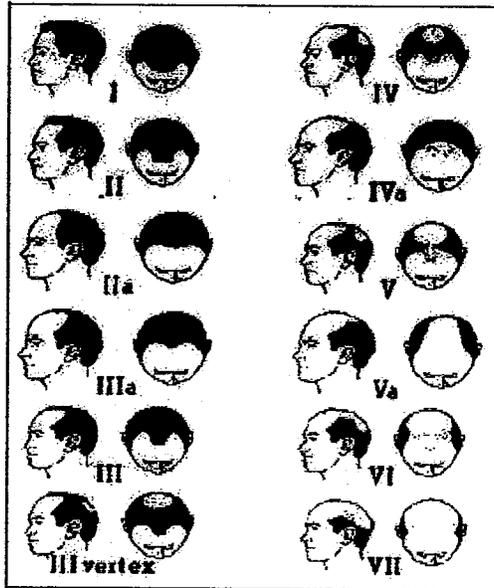


Figure 1. Hamilton-Norwood patterns of hair loss¹⁰

Appears This Way
On Original

STUDY ENDPOINT REVIEW

3.2 Subject questionnaire from Pfizer Protocol MINOB-9140-006

PLEASE LOOK AT THE POLAROID PHOTOGRAPHS OF THE VERTEX REGION OF YOUR HEAD. You will be rating your hair loss condition as of today compared to your screening visit hair loss condition.

Overall, how do you rate the HAIR LOSS CONDITION in the vertex region of your head, TODAY, WEEK 16 compared to SCREENING (beginning of the study), based on the photographs?

_____ 3 = Significantly Improved

_____ 2 = Moderately Improved

_____ 1 = Slightly Improved

_____ 0 = No Change

_____ -1 = Slightly worse

_____ -2 = Moderately worse

_____ -3 = Significantly worse

Appears This Way
On Original

STUDY ENDPOINT REVIEW

4 REFERENCES

- [1] NDA 21-812 Serial No. 0010, Rogaine® (minoxidil 5% foam) submitted by Pfizer on 23 March 2005.

Drafted 10/21/05 js

Concur 10/21/05 lb

Appears This Way
On Original

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

/s/

Jane A. Scott
10/26/2005 05:42:12 PM
UNKNOWN

Laurie Burke
10/27/2005 04:27:36 PM
INTERDISCIPLINARY

Appears This Way
On Original

Pfizer Consumer Healthcare
Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000



Consumer Healthcare

October 13, 2005

Curtis Rosebraugh, M.D., Acting Director
Division of Nonprescription Clinical Evaluation (HFD-560)
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 21-812
Men's Rogaine® Extra Strength 5% Minoxidil Topical Foam

Subject: Amendment to Pending Application
Safety Information

Dear Dr. Rosebraugh:

Reference is made to the above noted pending Original New Drug Application submitted on March 23, 2005 in Common Technical Document (CTD) format for Rogaine® Extra Strength (Minoxidil 5%) Topical Foam for over-the-counter (OTC) treatment of androgenetic alopecia of the vertex in men, and to the Agency's subsequent request for additional safety information to complete their review of this application.

Enclosed please find the items listed below.

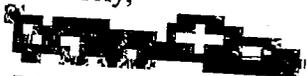
1. The Final Abbreviated Study Report: 5% Minoxidil Foam; Protocol MINOB-9140-006-Open Label; A Double-Blind, Randomized, Placebo-Controlled Trial of the Efficacy and Safety of 5% Minoxidil Foam in the Treatment of Androgenetic Alopecia in Males - Open Label Safety Phase
2. Revised ISS End-of-Text Tables and CRT's to include information from the Final Abbreviated Study Report: 5% Minoxidil Foam; Protocol MINOB-9140-006-Open Label Safety Phase
3. A Post-Marketing Safety Update Report covering the time period from August 1, 2004 through May 31, 2005

The Case Report Forms (CRF's), and Case Report Tabulations (CRT's) for this Amendment are being provided in electronic format. In accordance with the Guidance for Industry, Providing Regulatory Submissions in Electronic Format, General Considerations, a CD-ROM of the CRF's and CRT's in SAS® Transport format is included with the Archival copy of the application. These files were scanned with McAfee VirusScan Enterprise Version 8.0.0, Virus Definition 4603, Scan Engine 4400, and are virus free.

This submission contains confidential/trade secret information to which all claims of privilege and confidentiality are asserted in both statutory and common law. Further dissemination may only be made with the express written permission of Pfizer Inc.

Please contact me at the number below should you have any questions concerning this information.

Sincerely,



Dina Russello
Director Regulatory Affairs
(973) 385-4909

cc: Tia Frazier, Regulatory Project Manager

Appears This Way
On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT

Pharmacia & Upjohn, a Pfizer Company

DATE OF SUBMISSION

10/11/05

TELEPHONE NO. (Include Area Code)

(973) 385-4909

FACSIMILE (FAX) Number (Include Area Code)

(973) 385-4300

APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):

Pfizer, Inc.
201 Tabor Road
Morris Plains, NJ 07950

AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE

Dina Russello, Director
Global Regulatory Affairs
Pfizer Consumer Healthcare
201 Tabor Road, Morris Plains, NJ 07950

RECEIVED
OCT 12 2005

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 21-812

ESTABLISHED NAME (e.g., Proper name, USP/USAN name)

5% Minoxidil Topical Foam

PROPRIETARY NAME (trade name) IF ANY

Men's Rogaine Extra Strength

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)

2,4 pyrimidinediamine-6-(1-piperidinyl)-3-oxide

CODE NAME (If any)

DOSAGE FORM:

Topical Foam

STRENGTHS:

5%

ROUTE OF ADMINISTRATION:

Topical

(PROPOSED) INDICATION(S) FOR USE:

Hair Regrowth Treatment

APPLICATION DESCRIPTION

APPLICATION TYPE

(check one)

NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)

BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE

505 (b)(1)

505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug

Holder of Approved Application

TYPE OF SUBMISSION (check one)

ORIGINAL APPLICATION

AMENDMENT TO PENDING APPLICATION

RESUBMISSION

PRESUBMISSION

ANNUAL REPORT

ESTABLISHMENT DESCRIPTION SUPPLEMENT

EFFICACY SUPPLEMENT

LABELING SUPPLEMENT

CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT

OTHER

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

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY

CBE

CBE-30

Prior Approval (PA)

REASON FOR SUBMISSION

Submission of new patent information

PROPOSED MARKETING STATUS (check one)

PRESCRIPTION PRODUCT (Rx)

OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED

1

THIS APPLICATION IS

PAPER

PAPER AND ELECTRONIC

ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)

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

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

This application contains the following items: (Check all that apply)

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

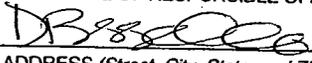
CERTIFICATION

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

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

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

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.
Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 		TYPED NAME AND TITLE Dina Russello, Director Regulatory Affairs	DATE: 10/11/05
ADDRESS (Street, City, State, and ZIP Code) 201 Tabor Road, Morris Plains, NJ 07950		Telephone Number (973) 385-4909	

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

Department of Health and Human Services
 Food and Drug Administration
 CDER, HFD-99
 11 Rockville Pike
 Rockville, MD 20852-1448

Food and Drug Administration
 CDER (HFD-94)
 12229 Wilkins Avenue
 Rockville, MD 20852

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

**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

21-812

NAME OF APPLICANT / NDA HOLDER

Pharmacia & Upjohn Co.
A Pfizer Company

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)

MEN'S ROGAINE EXTRA STRENGTH TOPICAL FOAM

ACTIVE INGREDIENT(S)

minoxidil

STRENGTH(S)

5%

DOSAGE FORM

Topical Foam

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

6946120

b. Issue Date of Patent

9/20/2005

c. Expiration Date of Patent

4/20/2019

d. Name of Patent Owner
Connetics Australia Pty. Ltd.
c/o General Counsel
Connetics Corp.

Address (of Patent Owner)

3160 Porter Drive

City/State

Palo Alto, CA

ZIP Code

94304

FAX Number (if available)

Telephone Number

650-843-2800

E-Mail Address (if available)

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.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

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

Yes

No

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

Yes

No

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

2. Drug Substance (Active Ingredient)

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

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

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b)? 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.)? 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.)? 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) 19 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.) Claim 19 is directed to a method of treating hair loss by applying the product for which approval is being sought to the scalp. The proposed consumer product information describes the product as being indicated for the regrowth of hair in men who have hair loss or thinning hair by application to the scalp, and so is covered by the claim.

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

Bruce A Pokras

10/3/2005

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
Bruce A. Pokras

Address
201 Tabor Road

City/State
Morris Plains, NJ

ZIP Code
07950

Telephone Number
(973) 385-5399

FAX Number (if available)
(973) 385-7330

E-Mail Address (if available)
bruce.a.pokras@pfizer.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.

Appears This Way
On Original

Teleconference Meeting Minutes

MEETING DATE: August 25, 2005
TIME: 11:15AM-12:10PM
LOCATION: Teleconference
APPLICATION: NDA 21-812
DRUG NAME: Rogaine Topical Aerosol
TYPE OF MEETING: C (FDA requested meeting)

MEETING CHAIR: Dr. Markham C. Luke

MEETING RECORDER: Tia Frazier, R.N., M.S.

FDA ATTENDEES:

Division of Dermatologic and Dental Drug Products
Markham C. Luke, M.D., Ph.D., Medical Team Leader
Mohamed A. Al Osh, Ph.D., Statistical Team Leader
Steven Thomson, Statistical Reviewer

Office of Nonprescription Products
Division of Nonprescription Clinical Evaluation
Daiva Shetty, M.D., Medical Officer
Andrea Leonard Segal, M.D., Medical Team Leader
Curtis Rosebraugh, M.D., M.P.H., Director
Tia Frazier, R.N., M.S., Project Manager

EXTERNAL CONSTITUENT ATTENDEES:

Regulatory Affairs
Dina Russello, Director
Ray Dann, Regulatory Consultant
Mike Bailey, Senior Director

Medical Affairs
Bruce Kohut, Senior Director
Rita Wanser, Associate Director
Carlos Quiza, Senior Clinical Scientist

Statistics and Data Management
Paul Zhang, Senior Manager

BACKGROUND:

At the end-of-Phase 2 meeting on January 16, 2003, FDA recommended co-efficacy endpoints of non-vellus hair counts and subject assessment of treatment benefit. The sponsor chose to use endpoints that differed from those previously recommended in only one pivotal study submitted with their pending NDA 21-812. FDA had also recommended that the sponsor compare the

techniques used to assess hair regrowth and that there was concern regarding the use of magnification to assess the hair growth endpoint.

Pfizer asserted their position that both the dot-mapping technique used for counting hair and the photographic magnification used for visualized hair counts were valid based on internal quality checks that they had conducted and was previously used for other applications for hair growth assessments. In response, the Agency requested the sponsor to submit any information which the sponsor could access, including publications and results of their early work which they referenced to during the meeting, in support of their assertions.

ACTION ITEMS:

Pfizer agreed to submit the following data and information:

1. Evidence that the hair counting techniques that they used excluded counts of vellus hair
2. Data supporting the existence of a correlation between the diameter of vellus hair and the cut-off hair diameter selected for this study (0.03mm)
3. Data supporting a correlation between subject self-assessment and hair counts stratified by treatment group

Pfizer also agreed to respond to the following questions and information requests that FDA sent by electronic mail to the sponsor on August 22, 2005 by September 6, 2005:

1. Investigate the association between the subject self assessment and hair counts including fitting statistical models, using ranks and box plots.
2. Investigate agreement between subject self assessment and median score of the expert panel review; and agreement between the subject self assessment and the score of each member of the expert panel review.
3. Provide individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr. ~~XXXXXXXXXXXX~~'S score.

The agency requested all requested analyses to address the FDA request of August 22, be carried out by treatment group (active, placebo) in addition to the overall analyses.

**Appears This Way
On Original**

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

/s/

Markham Luke
9/22/2005 10:10:00 AM

Appears This Way
On Original

- 5) Provide individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr _____'s score.

Please contact me at the number below should there be any questions regarding this submission.

Sincerely,

Dina Russello
Director Regulatory Affairs
(973) 385-4909

Cc: Tia Frazier, Regulatory Project Manager

Appears This Way
On Original

Attachment 1: Response to Clinical Endpoint Issues

- 1) What is the support for 0.03 mm (30 microns) as the appropriate diameter threshold for identifying non-vellus hairs?
- 2) How was the 5.7 fold final magnification determined to be the appropriate magnification at which only non-vellus hairs would be visualized and thereby counted in the hair counting methodology used?

Appears This Way
On Original

As noted in the Table 1.1 above, 0.03 mm is accepted as the upper limit diameter for vellus hairs. For example, Hordinsky et al states "Small hairs, with no pigment or medullary cavity, a diameter less than 0.03 mm, and a length of less than 1 cm, are classified as vellus (downy) hairs."¹ Whiting states that "Vellus hairs are inconspicuous and are 0.03 mm or less in diameter and often less than 1 cm in length and lack melanin and medulla."² Additional references^{3 4 5} are provided as well as the photocopies of the specific sections of these references for your review.

Based on the definitions outlined above and the literature references provided, Pfizer believes 0.03 mm is the appropriate diameter threshold for identifying visualized non-vellus hairs.

Appears This Way
On Original

References

¹ Hordinsky M, Sawaya M, Scher R: Atlas of Hair and Nails. Philadelphia, PA, Churchill Livingstone, 2000, p 10.

² Whiting DA: The Structure of the Human Hair Follicle. Fairfield, NJ, Canfield Publishing, 2004, p 5.

³ Unger W, Shapiro J: Hair Transplantation. Marcel Dekker, Inc, 2004, p 31-32.

⁴ Shapiro J: Hair loss: Principles of Diagnosis and Management of Alopecia . Martin Dunitz, 2002.

⁵ Olsen E (Editor): Disorders of Hair Growth Second Edition – McGraw-Hill Companies, Inc., 2003, p 7.

⁶ Kaufman K. et al. Finasteride in the treatment of men with androgenetic alopecia. JAAD 1998;39:578-589

⁷ Kohut B. et al. A Methodology Study Comparing Traditional 35mm Hair Counts to Automated Image Analysis Measurements, and Assessing Visualization Sensitivity of Hair Dyeing when Quantifying Hair Loss in Men and Women with Androgenetic Alopecia. Poster # 25. Presented at the European Hair Research Society Meeting Zurich July 2005.

⁸ Whiting DA: The Structure of the Human Hair Follicle. Fairfield, NJ, Canfield Publishing, 2004, p 26.

Appears This Way
On Original

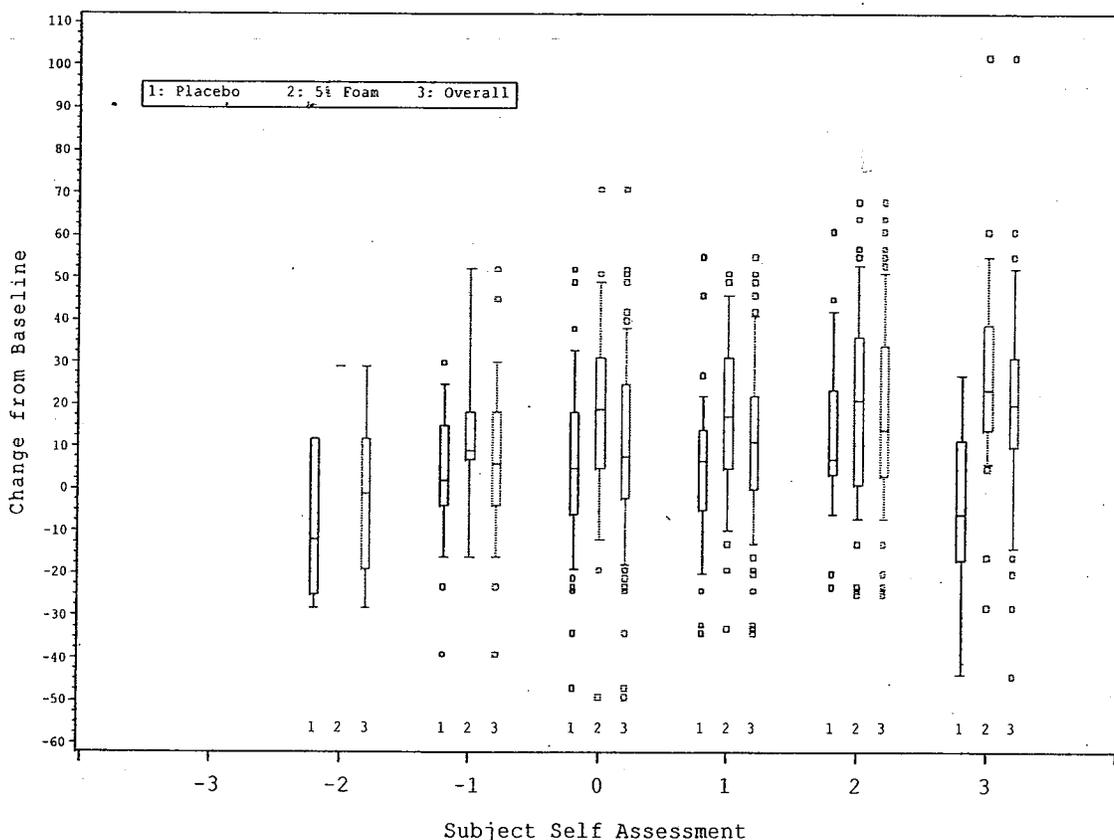
Attachment 2: Additional Analyses

- 1) The association between the subject self assessment and hair counts including fitting statistical models, using ranks and box plots.
- 2) The agreement between subject self assessment and median score of the expert panel review; and agreement between the subject self assessment and the score of each member of the expert panel review.
- 3) The individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr. _____'s score.

Appears This Way
On Original

Overall, a monotone upward trend is noticed with increased subject assessment. The average number of hair increased by 6.7/cm² even when subject self assessed as slightly worse. When subject self assessed as improved hair re-growth (score of 1, 2, or 3), the average hair count increased is at least 11.3 hairs/cm². For subjects who received 5% foam treatment and when they self noticed improved hair re-growth, the average incremental of hair count is at least 17 hairs/cm².

Box Plot of Change from Baseline in Hair Count vs Subject Assessment



Appears This Way
On Original

2. Investigate agreement between subject self assessment and median of score of the expert panel review; and agreement between the subject self assessment and the score of each member of the expert panel review.

The agreement between two ordinal variables is investigated by means of frequency distribution and the kappa statistic.

Table 2.1
Agreement between Subject Assessment(SS) & Median Score of the Expert Panel Review(EPR)

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	EPR	SS	EPR	SS	EPR
-2=Moderately Worse	8		1		9	
-1=Slightly Worse	25	4	10		35	4
0=No Change	56	134	32	94	88	228
1=Slightly Improved	36	8	41	55	77	63
2=Moderately Improved	28	1	47	14	75	15
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0374		0.1289		0.1038	

(a) Kappa was calculated, using Proc freq, based on complete or square data in each treatment group.

Table 2.2
Agreement between Subject Assessment(SS) and Dr. _____'s Score

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	Dr.	SS	Dr.	SS	Dr.
-2=Moderately Worse	8	1	1		9	1
-1=Slightly Worse	25	11	10	7	35	18
0=No Change	56	127	32	112	88	239
1=Slightly Improved	36	7	41	39	77	46
2=Moderately Improved	28	1	47	5	75	6
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0296		0.0495		0.0506	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Table 2.3
Agreement between Subject Assessment(SS) and Dr. _____'s Score

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	Dr.	SS	Dr.	SS	Dr.
-2=Moderately Worse	8		1		9	
-1=Slightly Worse	25	7	10		35	7
0=No Change	56	118	32	73	88	191
1=Slightly Improved	36	22	41	65	77	87
2=Moderately Improved	28		47	25	75	25
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0786		0.1337		0.1221	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Response to FDA Request for Information – Attachment 2: Additional Analyses

Table 2.4
 Agreement between Subject Assessment (SS) and Dr. _____'s Score

	Placebo (N=172)		5% Foam (N=180)		Overall (N=352)	
	SS	Dr. _____	SS	Dr. _____	SS	Dr. _____
-2=Moderately Worse	8	1	1		9	1
-1=Slightly Worse	25	4	10		35	4
0=No Change	56	124	32	93	88	217
1=Slightly Improved	36	17	41	50	77	67
2=Moderately Improved	28	1	47	20	75	21
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0244		0.1138		0.0858	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Overall, subject self assessment is more optimistic than expert's assessment, and as expected, subject assessment has larger variation than expert's assessment.

3. Provide individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr. _____ score.

The agreement between pairwise experts and among three experts are investigated by means of frequency distribution, pairwise kappa statistic and multiple rater kappa statistic.

Table 3.1
 Agreement between Dr. _____ and Dr. _____ and Dr. _____

	Placebo (N=172)			5% Foam (N=180)			Overall (N=352)		
	1	2	3	1	2	3	1	2	3
-2=Moderately Worse	1						1		
-1=Slightly Worse	11	7	4	7			18	7	4
0=No Change	127	118	124	112	73	93	239	191	217
1=Slightly Improved	7	22	17	39	65	50	46	87	67
2=Moderately Improved	1		1	5	25	20	6	25	21
Missing	25	25	25	17	17	17	42	42	42
Kappa (a)									
Dr. _____ vs Dr. _____	0.2285			0.1504			0.2135		
Dr. _____ vs Dr. _____	0.2258			0.2291			0.2507		
Dr. _____ vs Dr. _____	0.2764			0.4814			0.4683		
_____ vs _____ (b)	0.24801			0.26418			0.30956		

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

(b) Kappa (among multiple raters) were calculated using macro MAGREE from SAS.

Overall, Dr. [redacted] gave more conservative scores than Dr. [redacted] and Dr. [redacted]. The overall agreement with Dr. [redacted] is $\kappa=0.30956$ and without Dr. [redacted] is $\kappa=0.4683$.

Appears This Way
On Original

PROTOCOL: MINOB-9140-006

Data Listing (Page 1 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
PLACEBO	1001	101	2	1	1	0	1
		103	1	0	0	0	0
		106	0	-1	0	0	0
		108	2	0	-1	-2	-1
		109	1	0	0	0	0
		110	1	0	0	0	0
		536	1	0	0	0	0
		537	0	0	0	0	0
		538	0	0	0	0	0
		116	2	0	0	0	0
	1002	119	2	2	1	2	2
		123	3	0	0	0	0
		126	3	0	0	0	0
		127	0	1	1	1	1
		129	0	0	0	0	0
		372	0	0	0	0	0
		375	-1	0	0	0	0
		378	2	0	0	0	0
		380	2	0	0	0	0
		383	0	0	0	0	0
	1003	384	2	0	0	0	0
		589	1	0	0	0	0
		133	1	0	0	0	0
		137	0	0	0	0	0
		138	2	0	1	0	0
		141	0	-1	0	0	0
		142	3	0	0	0	0
		143	-1	-1	0	0	0
		292	0	0	0	0	0
		298	0	-1	0	0	0
299	0	0	0	1	0		
303	0	0	0	0	0		

(continued)

Generated by program: l10_rating_score006.sas at 11:10, 30AUG2005

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
 NDA 21-812/S-0010/Sept 2, 2005
 Response to FDA Request for Information -- Attachment 2 -- Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 2 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Score of EPR	Median		
PLACEBO	1003	304	1	-1	0	0	0	0		
		305	0	-1	-1	0	-1	-1		
		309	3	0	1	0	0	0		
		311	1	0	0	1	0	0		
		315	0	0	0	0	0	0		
		317	-2	-1	0	0	0	0		
		320	0	0	0	0	0	0		
		321	2	0	0	0	0	0		
		444	2	0	1	0	0	0		
		450	1	0	0	0	0	0		
		451	0	0	0	0	0	0		
		455	0	0	0	0	0	0		
		149	0	0	0	0	0	0		
		1004	1004	154	1	0	1	0	0	0
				156	-1	0	0	0	0	0
				162	1	0	0	0	0	0
				163	-1	0	0	0	0	0
359	2			0	0	0	0	0		
360	-1			0	0	0	0	0		
361	1			0	0	0	0	0		
368	2			0	0	0	0	0		
369	1			0	0	0	0	0		
166	1			-1	0	0	0	0		
1005	1005	167	-1	0	0	0	0	0		
		168	3	0	0	0	0	0		
		180	-1	0	0	0	0	0		
		185	0	0	0	0	0	0		
		186	-1	0	0	0	0	0		
		191	0	0	0	0	0	0		
		192	0	0	0	0	0	0		
		195	2	0	0	0	0	0		
		429	0	0	0	0	0	0		
		430	1	0	0	0	0	0		
1006	1006	430	1	0	0	0	0	0		

(continued)

Generated by program: l10_rating_score0006.sas at 11:10,30AUG2005

PROTOCOL: MINOB-9140-006

Data Listing (Page 3 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
PLACEBO	1006	439	3	0	0	1	0
		440	0	0	0	0	0
		442	1	0	0	0	0
	1007	592	1	0	0	0	0
		196	1	1	1	0	0
		200	-1	0	0	1	0
		202	-1	0	0	-1	0
		206	0	0	0	0	0
		209	0	0	-1	0	0
		490	0	0	0	0	0
1008		491	-2	0	0	-1	0
		493	0	0	0	0	0
		494	0	0	0	0	0
		496	0	0	0	0	0
		565	0	0	0	0	0
		567	-2	0	0	0	0
		214	0	0	0	1	0
		215	0	0	0	0	0
		216	-1	0	0	0	0
		221	-1	0	0	0	0
1009		223	2	-1	0	0	0
		227	0	0	0	0	0
		406	2	0	0	0	0
		409	0	0	0	0	0
		411	1	0	0	0	0
		413	2	0	0	1	0
		416	-2	0	0	0	0
		417	1	0	0	0	0
		541	-1	0	-1	0	0
		543	0	0	0	0	0
545	1	1	0	0	0		
230	-1	1	1	1	1		
231	1	-1	-1	-1	-1		

(continued)

Generated by program: l10_rating_score0006.sas at 11:10,30AUG2005

PROTOCOL: MINOB-9140-006

Data Listing (Page 4 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
PLACEBO	1009	232	-1	0	0	0	0
		244	1	0	0	0	0
		246	-1	0	0	0	0
		251	0	0	0	0	0
		254	2	0	1	1	1
		256	0	0	0	0	0
		259	2	0	0	0	0
		327	1	1	0	0	0
		328	-1	0	0	0	0
		331	0	0	0	0	0
	1010	332	-1	0	0	0	0
		336	0	1	1	1	1
		337	1	0	0	0	0
		341	-1	0	1	0	0
		344	0	0	0	0	0
		345	3	0	0	1	0
		352	-1	0	-1	0	0
		354	-1	0	0	0	0
		355	1	0	0	0	0
		388	0	0	0	0	0
1011	393	-2	0	0	0	0	
	395	-1	0	0	0	0	
	397	2	0	0	1	0	
	262	0	0	0	0	0	
	265	-2	0	0	0	0	
	269	1	0	1	0	0	
	273	3	0	1	0	0	
	275	-2	0	0	0	0	
	276	0	0	0	0	0	
	281	0	0	0	0	0	
1012	283	-1	0	0	0	0	
	286	0	0	0	0	0	
	288	2	0	1	1	1	

Generated by program: l10_rating_score006.sas at 11:10,30AUG2005 (continued)

PROTOCOL: MINOB-9140-006

Data Listing (Page 5 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
PLACEBO	1012	291	1	0	0	0	0
		477	0	0	0	0	0
		483	2	0	1	0	0
		600	1	0	1	1	1
		601	0	0	0	0	0
	1013	239	1	0	0	0	0
		461	2	0	0	1	0
		465	2	0	0	0	0
		466	1	0	0	0	0
		470	0	0	1	0	0
		473	2	0	0	0	0
		474	1	0	0	0	0
		572	1	0	0	0	0
		573	2	0	0	0	0
		574	1	1	1	1	1
581	3	0	0	0	0		
1014	583	0	0	1	0	0	
	586	2	0	0	0	0	
	501	0	0	0	0	0	
	507	1	0	-1	0	0	
	510	0	0	0	0	0	
	513	0	0	0	0	0	
	515	1	0	0	0	0	
	516	0	0	0	0	0	
	517	-1	-2	-1	-1	-1	
	522	2	1	0	0	0	
525	-1	0	0	0	0		
527	-2	0	0	0	0		
530	2	0	0	0	0		
557	0	0	0	0	0		
560	0	0	0	0	0		
562	0	0	0	0	0		
1001	1001	2	1	1	1	1	

(continued)

Generated by program: l10_rating_score0006.sas at 11:10, 30AUG2005

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
 NDA 21-812/S-0010/Sept 2, 2005
 Response to FDA Request for Information - Attachment 2 - Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 6 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr. 1	Dr. 2	Dr. 3	Dr. 4	Dr. 5	Median Score of EPR
5% TOPICAL MINOXIDIL FOAM	1001	102	2	1	2	1	1	1	1
		104	0	0	1	1	0	0	1
		111	0	0	0	0	0	0	0
		112	1	0	0	0	0	0	0
		113	3	0	0	0	0	0	0
		532	2	0	1	1	0	0	0
		533	3	1	2	2	2	2	2
	1002	534	2	0	0	0	0	0	0
		117	3	0	0	0	0	0	0
		118	1	1	1	1	0	0	1
		120	2	0	0	0	0	0	0
		124	2	1	2	1	1	1	1
		125	2	0	0	0	0	0	0
		373	3	0	0	0	0	0	0
		374	3	1	1	1	1	1	1
		376	3	0	0	0	0	0	0
		381	0	0	0	0	0	0	0
1003	382	3	0	0	0	0	0	0	
	385	2	1	1	1	1	1	1	
	132	2	0	1	1	0	0	0	
	134	0	0	2	2	0	0	0	
	135	1	0	0	0	0	0	0	
	140	3	2	1	1	1	1	1	
144	0	0	0	0	0	0	0		
293	3	0	0	1	1	0	0		
294	0	0	0	0	0	0	0		
295	2	0	1	1	1	0	0		
300	1	-1	1	1	1	0	0		
301	1	0	0	0	0	0	0		
302	-1	-1	0	0	0	0	0		
308	3	1	1	1	1	0	1		
310	1	-1	0	0	0	0	0		
312	2	0	0	0	0	1	0		

(continued)

Generated by program: l10_rating_score0006.sas at 11:10,30AUG2005

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
 NDA 21-812/S-0010/Sept 2, 2005
 Response to FDA Request for Information - Attachment 2 - Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 7 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
5% TOPICAL MINOXIDIL FOAM	1003	316	2	0	0	0	0
		318	2	1	1	2	1
		319	3	0	0	0	0
		445	2	0	0	0	0
		446	3	0	0	0	0
		447	2	0	2	1	1
		452	2	0	0	0	0
		453	1	0	0	0	0
		454	1	0	0	0	0
		150	-1	0	0	0	0
		151	3	0	1	0	0
		152	3	0	0	0	0
		157	3	0	1	1	1
		159	1	0	0	0	0
		356	1	0	1	0	0
357	1	0	0	0	0		
1005	1006	358	1	0	0	0	0
		364	0	0	0	0	
		365	3	0	1	0	
		366	1	0	0	0	
		164	0	0	1	1	
		165	1	0	1	1	
		169	1	0	1	1	
		181	1	0	1	1	
		182	0	1	1	1	
		183	0	0	0	0	
1006	1006	188	-2	0	0	0	
		189	1	0	1	1	
		190	3	0	1	1	
		428	2	1	2	1	
		431	2	1	0	0	
		432	-1	-1	0	0	
		436	1	1	1	1	

(continued)

Generated by program: l10_rating_score0006.sas at 11:10, 30AUG2005

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
 NDA 21-812/S-0010/Sept 2, 2005
 Response to FDA Request for Information -- Attachment 2 -- Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 9 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Median Score of EPR
5% TOPICAL MINOXIDIL FOAM	1009	229	0	1	1	0	1
		233	0	0	1	1	1
		245	0	0	0	0	0
		247	0	0	0	0	0
		252	0	0	0	0	0
		253	2	0	1	1	1
		255	2	0	1	0	0
		324	0	0	0	0	0
		325	3	0	0	0	0
		326	-1	0	0	0	0
		333	2	0	2	2	2
		334	0	1	2	2	2
		335	-1	1	1	1	1
		340	1	0	1	1	1
		343	3	2	2	2	2
	348	1	1	2	1	1	
	349	1	1	1	1	1	
	350	1	0	2	1	1	
	389	3	-1	2	2	2	
	390	3	0	2	2	2	
	391	-1	0	0	0	0	
	396	-1	-1	0	0	0	
	398	2	2	2	2	2	
	260	3	0	0	0	0	
	261	0	0	0	1	1	
	263	2	1	2	2	2	
	268	2	0	0	0	0	
	270	2	-1	0	0	0	
	420	3	1	0	0	0	
	421	1	0	1	1	1	
	277	-1	1	0	0	0	
	278	1	0	1	1	1	
	279	0	0	1	1	0	

(continued)

Generated by program: l10_rating_score0006.sas at 11:10.30AUG2005

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
 NDA 21-812/S-0010/Sept 2, 2005
 Response to FDA Request for Information - Attachment 2 - Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 10 of 11)
 SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

Treatment	Center	Subject ID	Subject Rating	Dr. Rating	Dr. Score	Median Score of EPR
5% TOPICAL MINOXIDIL FOAM	1012	285	1	0	1	2
		287	3	1	0	1
		476	2	1	0	1
		478	3	1	2	2
		479	2	2	2	2
		596	2	1	2	2
		597	1	0	1	1
		598	0	0	1	0
		236	2	0	0	0
		237	1	0	1	1
	1013	238	3	1	2	2
		460	2	0	0	1
		462	3	0	1	0
		463	3	0	0	0
		468	3	0	2	2
		469	3	1	2	1
		471	0	0	1	0
		575	1	0	1	1
		576	1	0	2	2
		577	1	0	1	1
1014	580	0	0	1	1	
	582	0	0	0	0	
	584	1	1	1	1	
	500	2	0	0	0	
	502	1	0	0	0	
	503	3	0	0	1	
	508	1	0	1	1	
	509	1	0	0	0	
	511	3	0	1	0	
	518	2	1	1	1	
519	2	1	2	0		
520	0	0	0	0		
524	3	1	0	0		

Generated by program: i10_rating_score0006.sas at 11:10,30AUG2005

(continued)

Men's Rogaine Extra Strength 5% Minoxidil Topical Foam
NDA 21-812/S-0010/Sept 2, 2005
Response to FDA Request for Information - Attachment 2 - Additional Analyses

PROTOCOL: MINOB-9140-006

Data Listing (Page 11 of 11)
SUBJECT RATING OF TREATMENT BENEFIT AND EXPERT PANEL REVIEW (EPR)

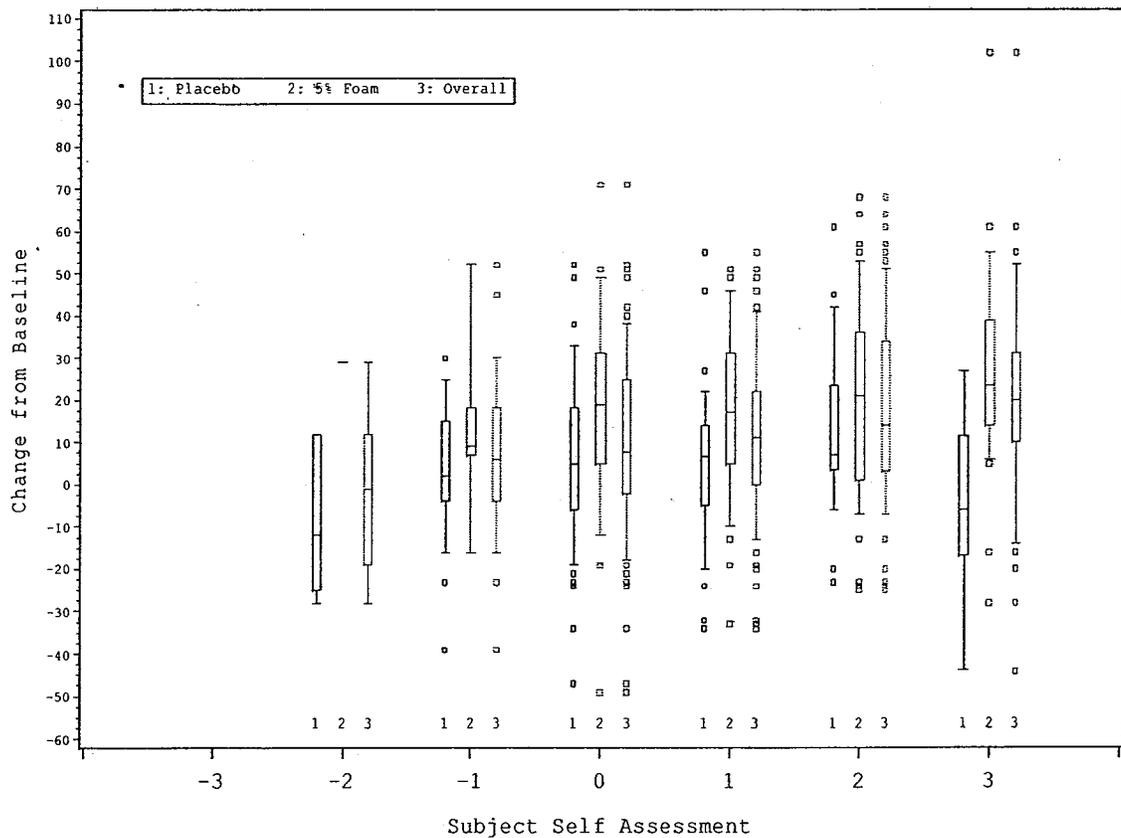
Treatment	Center	Subject ID	Subject Rating	Dr.	Dr.	Dr.	Score of EPR	Median
5% TOPICAL MINOXIDIL FOAM	1014	526	1	0	0	0	0	0
		528	2	0	1	0	0	0
		556	0	0	1	0	0	0
		558	1	1	1	1	1	1
		559	1	0	0	0	0	0

Generated by program: l10_rating_score0006.sas at 11:10,30AUG2005

Appears This Way
On Original

Overall, a monotone upward trend is noticed with increased subject assessment. The average number of hair increased by $6.7/\text{cm}^2$ even when subject self assessed as slightly worse. When subject self assessed as improved hair re-growth (score of 1, 2, or 3), the average hair count increased is at least $11.3 \text{ hairs}/\text{cm}^2$. For subjects who received 5% foam treatment and when they self noticed improved hair re-growth, the average incremental of hair count is at least $17 \text{ hairs}/\text{cm}^2$.

Box Plot of Change from Baseline in Hair Count vs Subject Assessment



Appears This Way
On Original

2. Investigate agreement between subject self assessment and median of score of the expert panel review; and agreement between the subject self assessment and the score of each member of the expert panel review.

The agreement between two ordinal variables is investigated by means of frequency distribution and the kappa statistic.

Table 2.1
 Agreement between Subject Assessment(SS) & Median Score of the Expert Panel Review(EPR)

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	EPR	SS	EPR	SS	EPR
-2=Moderately Worse	8		1		9	
-1=Slightly Worse	25	4	10		35	4
0=No Change	56	134	32	94	88	228
1=Slightly Improved	36	8	41	55	77	63
2=Moderately Improved	28	1	47	14	75	15
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0374		0.1289		0.1038	

(a) Kappa was calculated, using Proc freq, based on complete or square data in each treatment group.

Table 2.2
 Agreement between Subject Assessment(SS) and Dr. _____'s Score

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	Dr. _____	SS	Dr. _____	SS	Dr. _____
-2=Moderately Worse	8	1	1		9	1
-1=Slightly Worse	25	11	10	7	35	18
0=No Change	56	127	32	112	88	239
1=Slightly Improved	36	7	41	39	77	46
2=Moderately Improved	28	1	47	5	75	6
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0296		0.0495		0.0506	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Table 2.3
 Agreement between Subject Assessment(SS) and Dr. _____'s Score

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	Dr. _____	SS	Dr. _____	SS	Dr. _____
-2=Moderately Worse	8		1		9	
-1=Slightly Worse	25	7	10		35	7
0=No Change	56	118	32	73	88	191
1=Slightly Improved	36	22	41	65	77	87
2=Moderately Improved	28		47	25	75	25
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0786		0.1337		0.1221	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Table 2.4
Agreement between Subject Assessment (SS) and Dr. [redacted] s Score

	Placebo		5% Foam		Overall	
	(N=172)		(N=180)		(N=352)	
	SS	Dr. [redacted]	SS	Dr. [redacted]	SS	Dr. [redacted]
-2=Moderately Worse	8	1	1		9	1
-1=Slightly Worse	25	4	10		35	4
0=No Change	56	124	32	93	88	217
1=Slightly Improved	36	17	41	50	77	67
2=Moderately Improved	28	1	47	20	75	21
3=Significantly Improved	9		39		48	
Missing	10	25	10	17	20	42
Kappa (a)	0.0244		0.1138		0.0858	

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

Overall, subject self assessment is more optimistic than expert's assessment, and as expected, subject assessment has larger variation than expert's assessment.

3. Provide individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr. [redacted] score.

The agreement between pairwise experts and among three experts are investigated by means of frequency distribution, pairwise kappa statistic and multiple rater kappa statistic.

Table 3.1
Agreement between Dr. [redacted] and Dr. [redacted] and Dr. [redacted]

	Placebo			5% Foam			Overall		
	(N=172)			(N=180)			(N=352)		
	Dr. [redacted]								
-2=Moderately Worse	1		1				1		1
-1=Slightly Worse	11	7	4	7			18	7	4
0=No Change	127	118	124	112	73	93	239	191	217
1=Slightly Improved	7	22	17	39	65	50	46	87	67
2=Moderately Improved	1		1	5	25	20	6	25	21
Missing	25	25	25	17	17	17	42	42	42
Kappa (a)									
Dr. [redacted] vs Dr. [redacted]	0.2285			0.1504			0.2135		
Dr. [redacted] vs Dr. [redacted]	0.2258			0.2291			0.2507		
Dr. [redacted] vs Dr. [redacted]	0.2764			0.4814			0.4683		
[redacted] vs [redacted] vs [redacted] (b)	0.24801			0.26418			0.30956		

(a) Kappa were calculated, using Proc freq, based on complete or square data in each treatment group.

(b) Kappa (among multiple raters) were calculated using macro MAGREE from SAS.

Overall, Dr. [redacted] gave more conservative scores than Dr. [redacted] and Dr. [redacted]. The overall agreement with Dr. [redacted] is $\kappa=0.30956$ and without Dr. [redacted] is $\kappa=0.4683$.

Appears This Way
On Original

REQUEST FOR CONSULTATION

TO (Office/Division): Division of Pediatric Drug Development
Counter-Terrorism
Lisa Mathis, M.D., Director, Division of Pediatric
Drug Development

FROM (Name, Office/Division, and Phone Number of Requestor): Office of
Nonprescription Drug Products, Division of
Nonprescription Clinical Evaluation
Dr. Curtis Rosebraugh, M.D., Director

DATE May 19, 2005	IND NO.	NDA NO. 21-812	TYPE OF DOCUMENT waiver request	DATE OF DOCUMENT March 23, 2005
----------------------	---------	-------------------	------------------------------------	------------------------------------

NAME OF DRUG Men's Rogaine Extra Strength (minoxidil 5%) Topical Foam	PRIORITY CONSIDERATION High	CLASSIFICATION OF DRUG 3	DESIRED COMPLETION DATE December 14, 2005
--	--------------------------------	-----------------------------	--

NAME OF FIRM: Pharmacia and Upjohn, A Pfizer Company

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: In this NDA, the sponsor requested a full waiver from the requirement to conduct clinical studies in the pediatric population for androgenic alopecia. They submitted and reference the agency's denial of their July 25, 2000 request that we issue a Written Request letter calling for pediatric studies of androgenic alopecia in men less than 18 years old (attached). We know that clinicians prescribe Rogaine topical solutions for the treatment of alopecia areata in pediatric populations. Other available therapies for children with this condition such as steroid injections to the scalp introduce risks such as growth suppression and systemic and local adverse events. August, 2004, FDA advised NICHD that it recommended further study of minoxidil solution in children for the treatment of alopecia areata (list attached). Please provide your Division's feedback on whether or not to grant this request for a waiver for pediatric studies for the alopecia areata indication for this NDA.

SIGNATURE OF REQUESTOR _____	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

Appears This Way
On Original

not

MEMO REGARDING ROGAINE (MINOXIDIL) WAIVER REQUEST

Date: September 9, 2005

From: Rosemary Addy, MHS
Regulatory Health Project Manager,
Division of Pediatric Drug Development-
Office of Counter-Terrorism and Pediatric Drug Development

Through: Lisa Mathis, M.D.
Acting Director, Division of Pediatric Drug Development
Office of Counter-Terrorism and Pediatric Drug Development

To: Curtis Rosebraugh, M.D.
Director, Division of Nonprescription Clinical Evaluation
Office of Nonprescription Drug Products

Subject: Waiver Request for Men's Rogaine Extra Strength (minoxidil 5%)
Topical Foam (NDA-21-812)

The sponsor's application, NDA 21-812, is for a new dosage form of minoxidil for the already approved indication of hair regrowth treatment, also known as androgenetic alopecia. Pfizer has requested a full waiver from the requirement to conduct clinical studies in the pediatric population for this indication based on the fact that FDA previously refused to grant a Written Request for this indication, stating that the effectiveness of the product in the male population under age 18 years could be extrapolated from clinical studies conducted in adults.

The Division of Nonprescription Clinical Evaluation has asked for feedback from DPDD regarding whether a waiver can be granted for the treatment of alopecia areata in pediatric patients. They state that clinicians prescribe Rogaine topical solutions for the treatment of alopecia areata in pediatric populations. They further state that in August 2004, the FDA advised the National Institute of Child Health and Human Development (NICHD) that it recommended additional study of minoxidil solution in children for the treatment of alopecia areata. Studies to support this indication have not been submitted by the Sponsor, and minoxidil is not approved for this indication.

The Pediatric Research Equity Act (PREA) requires that applications submitted under section 505 of the Federal Food, Drug, and Cosmetic Act for a new active ingredient, a new indication, a new dosage form, a new dosing regimen, or a new route of administration must contain a pediatric assessment unless the assessment is waived or deferred. It should be noted that PREA is indication specific, and therefore, the required pediatric assessment must be for the indication for which the application is submitted.

This application is for a new dosage form, and therefore triggers PREA. None of the applications for Rogaine currently in house have been approved for alopecia areata in any population. The proposed indication for this application, hair regrowth treatment, does

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

/s/

Rosemary Addy
9/8/2005 05:19:18 PM
UNKNOWN

I made the change I emailed you about. If
you don't agree, we'll change it back.

Lisa Mathis
9/12/2005 11:01:17 AM
MEDICAL OFFICER
Concur

Appears This Way
On Original

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)**

DATE RECEIVED: May 18, 2005	DESIRED COMPLETION DATE: December 14, 2005	ODS CONSULT #: 05-0115
DATE OF DOCUMENT: March 23, 2005	PUDFA DATE: January 24, 2006	
TO: Curt Rosebraugh, MD Acting Director, Division of Nonprescription Clinical Evaluations Office of Nonprescription Drug Products HFD-105		
THROUGH: Tia-Frazier Project Manager HFD-105		
PRODUCT NAME: Men's Rogaine Extra Strength (Minoxidil Topical Foam) 5%	NDA SPONSOR: Pfizer	
NDA #: 21-812		
SAFETY EVALUATOR: Felicia Duffy, RN		
RECOMMENDATIONS: 1. DMETS has no objections to the use of the proprietary name, Men's Rogaine Extra Strength. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document. 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. DDMAC did not provide recommendations. DDMAC has no jurisdiction over OTC trade names.		
Denise Toyer, PharmD Deputy Director Division of Medication Errors and Technical Support Office of Drug Safety	Carol Holquist, RPh Director Division of Medication Errors and Technical Support Office of Drug Safety Phone: (301) 827-3242 Fax: (301) 443-9664	

Frazier, Tia

From: Frazier, Tia
Sent: Monday, August 22, 2005 5:27 PM
To: 'Dina Rusello (dina.russello@pfizer.com)'; 'Dina Russello (dina.russello@pfizer.com)'
Subject: Second set of information requests

Dear Dina,

We have the following information requests concerning your NDA 21-812.

Thank you, in advance, for your response. We are requesting a response by September 5, 2005.

Regards,

Tia Frazier

Information Requests

August 22, 2005

As hair count measurements were not carried out as visualized hair counts, as specified in the study protocol, the Agency is requesting that you submit the results of the following analyses to help us in interpreting efficacy findings of your drug Men's Rogaine Extra Strength Minoxidil 5% Topical Foam for androgenetic alopecia.

1. Investigate the association between the subject self assessment and hair counts including fitting statistical models, using ranks and box plots.
2. Investigate agreement between subject self assessment and median score of the expert panel review; and agreement between the subject self assessment and the score of each member of the expert panel review.
3. Provide individual score for each member of the expert panel review and investigate agreement between expert's scores with and without Dr. _____'s score.

We would appreciate very much receiving your response with two weeks of receiving this request as this would help us in completing our reviews for this application.

Tia Frazier, R.N., M.S.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Telephone: 301-827-2271
Fax: 301-827-2315
E-mail: fraziert@cder.fda.gov

Frazier, Tia

To: Dina Russello (dina.rusello@pfizer.com)
Subject: Info request
Contacts: Dina Russello

Dina,

The pharm-tox studies requested on 8/12 may be submitted as text-accessible PDF files. I have not yet followed up on whether we may ask for Word versions. I will follow up with you when I have an answer to that question.

I anticipate having several more questions about the hair counting methodologies for you in the next couple of days. The team wishes to put a 9/1/05 deadline for the responses to these, assuming we are not delayed in sending our questions to you. The team also requests a 9/1/05 deadline for responding to the questions posed in the electronic mail letter I sent to you on 8/12/05.

Regards,

Tia Frazier

Tia Frazier, R.N., M.S.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Telephone: 301-827-2271
Fax: 301-827-2315
E-mail: fraziert@cder.fda.gov

Appears This Way
On Original

Frazier, Tia

From: Frazier, Tia
Sent: Friday, August 12, 2005 4:06 PM
To: 'Dina Rusello (dina.russello@pfizer.com)'
Subject: FW: Questions and requests for information

Greetings, Dina,

The review team has the following questions and requests for information concerning the information you submitted on July 19, 2005:

1. What is the cutoff of diameter for hair measurement using dot mapping technique (smallest hair diameter measured)?
2. Could you please provide a reanalysis of the data using a hair counting technique that excludes hair with a diameter of less than 0.03 mm and an additional analysis excluding hair of less than 0.05 mm diameter?
3. Provide a graphic plot showing the distribution of hair diameters vs. counts for their given study population with a comparison between the different arms?
4. Provide a graphic plot showing the distribution of hair diameters vs. counts for the study population with a comparison between the different arms.

Thanks. I will forward these requests in a fax as well. Could you do me a favor by letting me know how long you think you'll need to respond to these questions and requests for more information?

Tia

Tia Frazier, R.N., M.S.

Regulatory Project Manager

Division of Nonprescription Clinical Evaluation

Office of Nonprescription Products

Telephone: 301-827-2271

Fax: 301-827-2315

E-mail: fraziert@cder.fda.gov

-----Original Message-----

From: Luke, Markham C
Sent: Friday, August 12, 2005 11:21 AM
To: Frazier, Tia
Cc: Kukich, Stanka; Thomson, Steven F; Huene, Phyllis A; Leonard Segal, Andrea; Rosebraugh, Curtis; Shetty, Daiva
Subject: RE: Pfizer's response to our questions

Hi Tia,

Thanks,
Markham

-----Original Message-----

From: Frazier, Tia
Sent: Monday, July 18, 2005 3:28 PM
To: Thomson, Steven F; Bashaw, Edward D; Bhavnagri, Vispi P; Blay, Roy A; Christl, Leah A; Holman, Matthew Ray; Huene, Phyllis A; Kukich, Stanka; Leonard Segal, Andrea; Luke, Markham C; Mainigi, Daivender K; Rosebraugh, Curtis; Shetty, Daiva; Smith, John L; Tavarezpagan, Jose; Tesch, Dianne
Cc: Hilfiker, David R
Subject: Pfizer's response to our questions

This attachment contains the company's responses to our questions regarding the chemistry and clinical sections of NDA 21-812.

<< File: Rogaine Response.pdf >>

Tia Frazier, R.N., M.S.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Telephone: 301-827-2271
Fax: 301-827-2315
E-mail: fraziert@cder.fda.gov

Appears This Way
On Original

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

/s/

Tia Frazier
8/16/2005 09:13:31 AM
CSO

Appears This Way
On Original

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Men's Rogaine Extra Strength 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 conducted⁴. An expert panel discussion was conducted to review all findings from the searches.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Men's Rogaine Extra Strength. 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. DDMAC comments are as follows: DDMAC has no jurisdiction over the OTC trade names. Therefore, we will not comment on OTC trade names.
2. The Expert Panel identified two proprietary names that were thought to have the potential for confusion with Men's Rogaine Extra Strength. These products are 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

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Men's Rogaine Extra Strength	Minoxidil Topical Foam: 5%	Apply to hair loss area twice daily.	
Men's Rogaine Extra Strength	Minoxidil Topical Solution: 5%	Apply to hair loss area twice daily.	LA/SA
Rogaine (Men's and Women's)	Minoxidil Topical Solution: 2%	Apply to hair loss area twice daily.	LA/SA

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

¹ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-05, and the electronic online version of the FDA Orange Book.

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

- c. The fourth bullet instructs the consumer “dispense the topical foam product” ~~into the palm of the hand~~. Yet, the corresponding illustration shows the product being dispensed onto the finger. Since the consumer is instructed to cool their fingers by rinsing them in cold water in the third bullet, and then instructed to use their fingers to spread the product in the fifth bullet, we recommend the fourth bullet be revised to instruct the consumer to dispense the product onto their fingertips and then refer them to the corresponding illustration.
- d. The fourth bullet also instructs the user that “the total amount of foam applied should not exceed half a capful”. We recommend the cap be incremented or marked to clearly show the half capful level. It may also be helpful to give the user another point of reference equivalent to half a capful (e.g., the total amount of foam should be about the size of a golf ball).
-
- e. The second question on page 15 address the issues of the product and the potential for unwanted hair growth. In particular, it addresses unwanted hair growth in women, yet this product is not indicated for women. This section goes on to give instructions on how to reduce the chances of unwanted hair growth. DMETS questions why this section does not re-instruct women not to use this product due to unwanted hair growth. In addition, Step 2 of this section states the following: “If you use your hands to apply Rogaine Extra Strength Foam, wash your hands well immediately afterwards.” Since the consumer is instructed to use their fingers to apply the product, the directions should be revised to instruct the consumer to wash their hands immediately after applying the product.

*Appears This Way
On Original*

IV. RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name Men's Rogaine Extra Strength. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
- B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
- C. DDMAC did not provide recommendations. DDMAC has no jurisdiction over OTC trade names.

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 301-827-1998.

Felicia Duffy, RN
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, RPh, MS
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appears This Way
On Original

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

/s/

Felicia Duffy
8/4/05 06:21:39 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
8/4/05 07:45:49 AM

DRUG SAFETY OFFICE REVIEWER

Denise Toyer
8/4/05 10:24:02 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
8/4/05 11:50:19 AM
DRUG SAFETY OFFICE REVIEWER

Appears This Way
On Original

MEMORANDUM OF TELECON

DATE: July 20, 2005

APPLICATION NUMBER: IND/NDA 21-812

BETWEEN:

Name: Dina Russello
Phone: 973-385-4909
Representing: Pharmacia and Upjohn, A Pfizer Company

AND

Name: Tia Frazier
Division of Nonprescription Clinical Evaluation, HFD-560

SUBJECT:

I telephoned Ms. Russello to confirm receipt of her July 8, 2005 NDA amendment to NDA 21-812 for Men's Rogaine Extra Strength Topical Foam (5% minoxidil topical aerosol). I confirmed FDA's understanding of the applicant's position that no significant issues warrant a labeling comprehension study. I informed Ms. Russello that FDA was not prepared to provide a response to their position on the need for a labeling comprehension study at this point in the review cycle. I informed Ms. Russello that their company's decision not to include such a study and position that one was not warranted would be a review issue. The conversation concluded cordially.

Tia Frazier
Regulatory Project Manager

Appears This Way
On Original

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

/s/

Tia Frazier
7/20/05 12:04:27 PM
CSO

Appears This Way
On Original



PFIZER, INC.

Facsimile Cover Sheet

TO: Tia Frazier
Company: CDER FDA
Phone: (301) 827-2271
Fax: 301-827-2315

FROM: Dina Russello
Company: Pfizer, Inc.
Global Regulatory Affairs
201 Tabor Road
Building 1 - '79N-3
Morris Plains, NJ 07950
Phone: 973-385-4909
Fax: 973-385-4300

Date: July 18, 2005
Pages including
this cover page: _____

Comment: Tia,
Per our conversation this afternoon, attached
please find responses to your questions faxed
on June 21, 2005. Please call me if you
have any question concerning this information.
Thanks
Dina

Confidential

This transmission is intended only for the use of the Addressee and may contain information that is confidential. If you are not the intended recipient, you are hereby notified that any dissemination, distributions or copying of the information contained in this facsimile is strictly unauthorized and prohibited. If you have received this facsimile in error, please notify us immediately by collect telephone call to the sender named above. Thank you.

Pfizer Consumer Healthcare

Pfizer Inc
201 Tabor Road
Morris Plains, NJ 07950
Tel 973 385 2000



Consumer Healthcare

July 19, 2005

Curtis Rosebraugh, M.D., Acting Director
Division of Nonprescription Clinical Evaluation (HFD-560)
Office of Nonprescription Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Re: NDA 21-812/ S-0007
Men's Rogaine® Extra Strength 5% Minoxidil Topical Foam

Subject: Response to FDA Request for Information

Dear Dr. Rosebraugh:

Please make reference to the above pending NDA and the June 21, 2005 fax from your Division containing three information requests as follows:

- 1. The sensitization study does not appear to have been performed with the minoxidil foam formulations or the vehicle formulation that were used in Study 006, as the formula numbers provided in the separate study reports are not the same. Please clarify.*

The active foam formulations used in the sensitization study (004) and in the phase 3 study (006) were the same. The report and the synopsis for study 006 contained an error wherein the formulation numbers for the foam and placebo formulations are reversed. The correct formulation numbers are P902942A00 for the 5% minoxidil foam and P902943A00 for the placebo foam. Corrected pages for the 006 study report (Module 5, Volume 4, Page 34) and the 006 synopsis (Module 2, Volume 1, page 143) will be issued.

The placebo vehicle formulations in studies 004 (P902946A00) and 006 (P902943A00) differed, because the placebo used in study 004 was unscented in order to evaluate the irritation/sensitization potential of minoxidil and each of 2 fragrances.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		Form Approved: OMB No. 0910-0338 Expiration Date: August 31, 2005 See OMB Statement on page 2.	
APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE (Title 21, Code of Federal Regulations, Parts 314 & 601)		FOR FDA USE ONLY	
		APPLICATION NUMBER	
APPLICANT INFORMATION			
NAME OF APPLICANT Pharmacia & Upjohn, A Pfizer Company		DATE OF SUBMISSION 7/19/05	
TELEPHONE NO. (Include Area Code) (973) 385-4909		FACSIMILE (FAX) Number (Include Area Code) 973-385-4300	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Pfizer Inc 201 Tabor Road Morris Plains, NJ 07950		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Dina R. Russello, Director Global Regulatory Affairs Pfizer Consumer Healthcare 201 Tabor Road Morris Plains, NJ 07950	
PRODUCT DESCRIPTION			
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) 21-812			
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) 5% Minoxidil Topical Foam		PROPRIETARY NAME (trade name) IF ANY Men's Rogaine Extra Strength *	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 2,4-pyrimidinediamine-6-(1-piperidinyl)-3-oxide		CODE NAME (if any)	
DOSAGE FORM: Topical Foam	STRENGTHS: 5%	ROUTE OF ADMINISTRATION: Topical	
(PROPOSED) INDICATION(S) FOR USE: Hair Regrowth Treatment			
APPLICATION DESCRIPTION			
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)			
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)			
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____			
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER			
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____			
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)			
REASON FOR SUBMISSION Response to FDA Request for Information			
PROPOSED MARKETING STATUS (check one) <input type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input checked="" type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)			
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC			
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.			
Drug Product Manufacturing, Packaging, Release/Stability Testing - _____ ready for PAI on or about June 1, 2005			
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)			
IND 50.063 Minoxidil Foam; NDA 19-501 Rogaine Regular Strength (2% Minoxidil) Topical Solution; NDA 20-834 Men's Rogaine Extra Strength (5% Minoxidil) Topical Solution: DMF _____, DMF _____, DMF _____, DMF _____			

This application contains the following items: (Check all that apply)

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

CERTIFICATION

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

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

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

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.
 Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT 	TYPED NAME AND TITLE Dina R. Russello, Director Regulatory Affairs	DATE: 7/19/05
ADDRESS (Street, City, State, and ZIP Code) 201 Tabor Road, Morris Plains, NJ 07950		Telephone Number (973) 385-4909

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

Department of Health and Human Services
 Food and Drug Administration
 CDER, HFD-99
 1401 Rockville Pike
 Rockville, MD 20852-1442

Food and Drug Administration
 CDER (HFD-94)
 12229 Wilkins Avenue
 Rockville, MD 20852

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

6 Page(s) Withheld

 Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-6

RECEIVED
AUG 22 2005

HFD-560/CDER

by email J. J.

1. What is the cutoff of diameter for hair measurement using dot mapping technique (smallest hair diameter measured)?

The cutoff diameter is 0.03 mm for the dot mapping technique used.

2. Could you please provide a reanalysis of the data using a hair counting technique that excludes hair with a diameter of less than 0.03 mm and an additional analysis excluding hair of less than 0.05 mm diameter?

Reanalysis of the data using diameter of hair as cut points is not possible using the photographs taken in the trial (MINO-9140-006). While the hair counting technique used permits the establishment of a lower threshold (0.03 mm), it does not permit direct measurement of individual hair diameter.

There are newer hair counting technologies that permit concurrent measurement of individual hair diameter and target area hair count. These other hair counting techniques were not included in this trial as the trial was designed to use an established, validated and published technique that was accepted by the Agency for the approval of both Propecia and Minoxidil products.

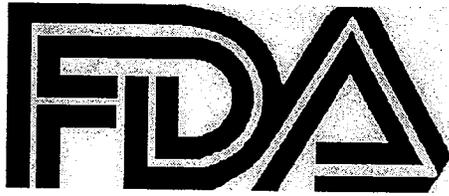
3. Provide a graphic plot showing the distribution of hair diameters vs. counts for their given study population with a comparison between the different arms?

Graphic plots showing distribution of hair diameters can not be provided since individual hair diameters can not be measured. See response to question 2 above.

4. Provide a graphic plot showing the distribution of hair diameters vs. counts for the study population with a comparison between the different arms.

Graphic plots showing distribution of hair diameters can not be provided since individual hair diameters can not be measured. See response to question 2 above.

Appears This Way
On Original



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE V

FACSIMILE TRANSMITTAL SHEET

DATE: June 21, 2005

To: Dina Russello	From: Tia Frazier
Company: Pfizer Consumer Healthcare	Division of Over-the-Counter Drug Products
Fax number: 973-385-4300	Fax number: 301-827-2315
Phone number: 973-385-4909	Phone number: 301-827-2271
Subject: Requests for Information	

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

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

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2222. Thank you.

Appears This Way
On Original



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-812

Pharmacia and Upjohn, A Pfizer Company
Attention: Dina R. Russello, Director
Global Regulatory Affairs
201 Tabor Road
Morris Plains, NJ 07950

Dear Ms. Russello:

Please refer to your March 23, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Men's Rogaine Extra Strength Topical Foam (5% minoxidil topical aerosol).

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on May 23, 2005 in accordance with 21 CFR 314.101(a).

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

1. A spectrum for this product in the ultraviolet-visible light range of _____, nm may not have been provided.

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

We request that you submit the following information:

1. Provide a spectrum for this product in the ultraviolet-visible light range of _____, or if already provided in the NDA, specify the location of this information.

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

NDA 21-812

Page 2

If you have any questions, call Tia Frazier, Regulatory Project Manager, at (301) 827-2271.

Sincerely,

{See appended electronic signature page}

Leah Christl, Ph.D.
Acting Supervisory Project Manager
Division of Nonprescription Clinical
Evaluation
Office of Nonprescription Products

Appears This Way
On Original

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

/s/

Leah Christl
5/24/05 09:50:34 AM

Appears This Way
On Original



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-812

Pfizer Consumer Healthcare
Pfizer Incorporated
Attention: Dina Russello
Director, Regulatory Affairs
201 Tabor Road
Morris Plains, New Jersey 07977

Dear Ms. Russello:

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

Name of Drug Product: Men's Rogaine Extra Strength Topical Foam (5% minoxidil topical aerosol)

Review Priority Classification: Standard (S)

Date of Application: March 23, 2005

Date of Receipt: March 24, 2005

Our Reference Number: NDA 21-812

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 23, 2005 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 24, 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 requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed, we will notify you whether we have waived the pediatric study requirement for this application.

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

NDA 21-812

Page 2

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

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

U.S. Postal Service:

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

Courier/Overnight Mail:

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

If you have any questions, call Tia Frazier, Regulatory Project Manager, at (301) 827-2271.

Sincerely,

{See appended electronic signature page}

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

Appears This Way
On Original

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

/s/

Leah Christl
5/23/05 12:51:41 PM

Appears This Way
On Original

REQUEST FOR CONSULTATION

TO (Division/Office):

Mail: ODS (Room 15B-08, PKLN Bldg.)

FROM: Tia Frazier, Project Manager

Office of Nonprescription Drug Products
Division of Nonprescription Clinical Evaluation

DATE
May 17, 2005

IND NO.

NDA NO.21-812

TYPE OF DOCUMENT NDA

DATE OF DOCUMENT March 23, 2005

NAME OF DRUG Men's Rogaine
Extra Strength

PRIORITY CONSIDERATION High

CLASSIFICATION OF DRUG
Chemical Type 3 (3S),
Hair regrowth Treatment

DESIRED COMPLETION DATE
December 14, 2005
(PDUFA goal-1/24/06)

NAME OF FIRM: Pfizer Consumer Healthcare

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): labeling review-see |
| <input type="checkbox"/> MEETING PLANNED BY | | comments for specific issues and |
| | | concerns |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- | | |
|--|---|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|---|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

- | | |
|--|--|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS: PDUFA DATE: 1/24/06
ATTACHMENTS: Draft Package Insert, Container and Carton Labels

Please provide feedback on the attached labeling submitted with NDA 21-812 for 5% minoxidil topical foam. The Divisions are concerned about the sponsor's inclusion of the terms "extra strength" in their proposed trade name for this product since their studies do not include comparisons between the proposed product and the approved regular strength (2% minoxidil topical solution) and extra strength product (minoxidil 5% topical solution).

SIGNATURE OF REQUESTER

METHOD OF DELIVERY (Check one)
x MAIL

HAND

SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER
-----------------------	------------------------

Appears This Way
On Original

11 Page(s) Withheld

 Trade Secret / Confidential

✓ Draft Labeling

 Deliberative Process

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

/s/

Curtis Rosebraugh
5/17/05 02:23:04 PM

Appears This Way
On Original

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 PKLN Rm. 6-34		FROM: Tia Frazier, Project Manager Office of Nonprescription Drug Products Division of Nonprescription Clinical Evaluation		
DATE May 16, 2005	IND NO.	NDA NO. 21-812	TYPE OF DOCUMENT NDA	DATE OF DOCUMENT March 23, 2005
NAME OF DRUG Men's Rogaine Extra Strength -	PRIORITY CONSIDERATION High		CLASSIFICATION OF DRUG Chemical Type 3 (3S), Hair regrowth Treatment	DESIRED COMPLETION DATE December 1, 2005 (PDUFA goal-1/24/06)
NAME OF FIRM: Pfizer Consumer Healthcare				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS: PDUFA DATE: 1/24/06 Archival IND/NDA 21-812 HFD-560/Division File HFD-560/RPM HFD-560 and 540/Reviewers and Team Leaders				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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

/s/

Curtis Rosebraugh
5/16/05 04:43:02 PM

Appears This Way
On Original



Consumer Healthcare

April 28, 2005

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

Attention: Charles Ganley, M.D., Director
Division of Over-the-Counter Drug Products (HFD-560)
Office of Drug Evaluation V

Re: NDA 21-812 - Amendment to Pending Application - Serial 0001
Men's Rogaine® Extra Strength Minoxidil 5% Topical Foam

Subject: Electronic Regulatory Submission For Archive
Module 2, Module 5 Volumes 13 and 14

Dear Dr. Ganley:

Please refer to NDA 21-812 for Minoxidil 5% Topical Foam dated March 23, 2005, which was submitted in paper and electronic format. In accordance with the request made by Ms. Tia Frazier on April 15, 2005, this submission provides 2 CD-ROM disks containing electronic versions of selected sections of that NDA as follows.

Disk # 1: Module 2 - Summaries

Disk # 2: Module 5 Volumes 13 and 14 - Integrated Summary of Safety

The files have been scanned with McAfee Virus Scan, Version 4.5.1 SP1, Virus Definition 4.0.4443 Scan Engine 4.4.00 and are virus free.

If there are any questions regarding this submission, please contact me at 973-385-4909.

Sincerely,

A handwritten signature in black ink, appearing to read "Dina R. Russello".

Dina R. Russello
Director Regulatory Affairs

Cc: Tia Frazier, Project Manager, DOTCDP

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-812

Supplement #

Efficacy Supplement Type SE-

Trade Name: Men's Rogaine Extra Strength Topical Foam
Established Name: 5% minoxidil topical aerosol
Strengths: 5%

Applicant: Pfizer Consumer Healthcare
Agent for Applicant: Dina Russello

Date of Application: March 23, 2005
Date of Receipt: March 24, 2005
Date clock started after UN: Not applicable
Date of Filing Meeting: May 12, 2005
Filing Date: May 23, 2005
Action Goal Date (optional): January 24, 2006

User Fee Goal Date: January 24, 2006

Indication(s) requested: Hair regrowth treatment

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

NOTE:

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

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

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

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

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

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

Version: 12/15/2004

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

If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO
If yes, explain:
- Does another drug have orphan drug exclusivity for the same indication? YES NO
- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

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

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES NO
- Does the submission contain an accurate comprehensive index? YES NO
- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:
- If an electronic NDA, does it follow the Guidance? N/A YES NO
If an electronic NDA, all forms and certifications must be in paper and require a signature.
Which parts of the application were submitted in electronic format?

Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A YES NO
- Is it an electronic CTD (eCTD)? N/A YES NO
If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO
- Exclusivity requested? YES, 3yrs Years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

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

- Financial Disclosure forms included with authorized signature? YES NO
(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y NO
- PDUFA and Action Goal dates correct in COMIS? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: 50,063
- End-of-Phase 2 Meeting(s)? Date(s) January 16, 2003 NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) _____ NO
If yes, distribute minutes before filing meeting.

Project Management

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

If Rx-to-OTC Switch application:

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

Clinical

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

Chemistry

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

Appears This Way
On Original

ATTACHMENT

MEMO OF FILING MEETING

DATE: May 12, 2005

BACKGROUND: This NDA proposes a minoxidil aerosol foam in a 5% concentration for the treatment of androgenic alopecia in adult males. The applicant already markets three FDA approved hair regrowth products: 1) 2% minoxidil solution for women 2) 2% solution for men and 3) 5% minoxidil solution (Extra Strength) for men. HFD-540 and the Office of Nonprescription Products are jointly reviewing this NDA submitted in CTD format.

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

ATTENDEES: included "Assigned Reviewers" below with the following exceptions: Tapash Ghosh attended for Edward Bashaw, Team Leader, Clinical Pharmacology/Biopharmaceutics. Leah Christl, Acting Supervisory Project Manager; John Smith, Chemistry Team Leader; Markham Luke, Medical Team Leader; and Margo Owens, Regulatory Project Manager were also in attendance.

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

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Daiva Shetty, Medical Officer
Secondary Medical:	Phylis Huene, Medical Officer
Statistical:	Steven Thompson, Statistical Reviewer
Pharmacology:	Daivender Mainigi, Pharmacology Reviewer
Statistical Pharmacology:	
Chemistry:	Vispi Bhavnagri, Chemistry Reviewer
Environmental Assessment (if needed):	
Biopharmaceutical:	Edward Bashaw, Biopharmaceutical Reviewer
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	
DSI:	Diane Tesch, Consumer Safety Officer
Regulatory Project Management:	Tia Frazier, Project Manager
Other Consults:	

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

CLINICAL FILE REFUSE TO FILE

- Clinical site inspection needed? YES NO
- Advisory Committee Meeting needed? YES, date if known _____ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A YES NO

CLINICAL MICROBIOLOGY N/A FILE REFUSE TO FILE

STATISTICS	N/A <input type="checkbox"/>	FILE <input checked="" type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
BIOPHARMACEUTICS		FILE <input checked="" type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
	• Biopharm. inspection needed?		YES <input type="checkbox"/> NO <input checked="" type="checkbox"/>
PHARMACOLOGY	N/A <input type="checkbox"/>	FILE <input checked="" type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
	• GLP inspection needed?		YES <input type="checkbox"/> NO <input checked="" type="checkbox"/>
CHEMISTRY		FILE <input checked="" type="checkbox"/>	REFUSE TO FILE <input type="checkbox"/>
	• Establishment(s) ready for inspection?		YES <input checked="" type="checkbox"/> NO <input type="checkbox"/>
	• Microbiology		YES <input type="checkbox"/> NO <input checked="" type="checkbox"/>

ELECTRONIC SUBMISSION:

Any comments: The CTD was submitted in paper with selected sections submitted in electronic format.

REGULATORY CONCLUSIONS/DEFICIENCIES:

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

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
 - No filing issues have been identified.
 - Filing issues to be communicated by Day 74. List (optional):
 1. Provide a spectrum for Rogaine foam in the ultraviolet-visible light range from _____, or if already provided in the NDA, specify the location of this information.

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Convey document filing issues/no filing issues to applicant by Day 74.

Tia Frazier, R.N., M.S.
Regulatory Project Manager, HFD-560

Appears This Way
On Original

Appendix A to NDA Regulatory Filing Review

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

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

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

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

Appears This Way
On Original

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

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

If "No," skip to question 3.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

If "No," skip to question 6.

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

- (b) Is the approved drug product cited as the listed drug? YES NO
6. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").
7. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO
8. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9)). YES NO
9. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES NO
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)
- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):
- 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s):

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

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

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

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

IND# _____ NO

OR

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

YES NO

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

YES NO

Appears This Way
On Original

5891

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Office/Division): **Mary Jean Kozma-Fornaro**
Division of Dermatologic and Dental Drug Products

FROM (Name, Office/Division, and Phone Number of Requestor): **Tia Frazier**
Division of Over-the-Counter Drug Products

DATE
4/21/04

IND NO.

NDA NO.
21-812

TYPE OF DOCUMENT
New Drug Application

DATE OF DOCUMENT
March 23, 2004

NAME OF DRUG
5% Minoxidil Topical Foam

PRIORITY CONSIDERATION
H

CLASSIFICATION OF DRUG
Type 3 (new dosage form)

DESIRED COMPLETION DATE
January 2, 2005

NAME OF FIRM: **Pharmacia & Upjohn, A Pfizer Company**

REASON FOR REQUEST

I. GENERAL.

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> .SOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|---|
| <input type="checkbox"/> CLINICAL | <input checked="" type="checkbox"/> NONCLINICAL |
|-----------------------------------|---|

COMMENTS / SPECIAL INSTRUCTIONS: Please review and comment on the adequacy of the pharmacology and toxicology studies submitted by the sponsor to support approval of 5% Minoxidil Topical Foam. Specifically, we seek your feedback on 1) the results of Study No. 403 (proof of concept study using macaque monkeys) 2) pharmacokinetics study of three ——— mousses using hamster and cadavar skin models 3) justification provided for 0.5% level of desoxyminoxidil in the foam product and 4) submitted non-clinical literature. Please comment on whether these submissions support approval of this NDA from your discipline's perspective. The volumes comprising the non-clinical section of this NDA (in CTD format) should already be in your possession. Please contact me at 301-827-2271 if you do not already have a set of volumes for this NDA.

SIGNATURE OF REQUESTOR
Tia Frazier, Regulatory Project Manager

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

MEMORANDUM OF MEETING MINUTES



Meeting Date: January 16, 2003 Time: 10:00 AM
Location: 9201 Corporate S200A
Application: IND 50, 063, 5 % Minoxidil Topical Foam (Mousse) -
Indication: Treatment of Androgenetic Alopecia
Meeting ID: 9712, End-of-Phase 2 Meeting
Sponsor: Pharmacia Consumer Healthcare
Meeting Chair: Jonathan Wilkin, M.D., Division Director, DDDDP, HFD-540
Meeting Recorder: Jacquelyn Smith, M.A., Regulatory Project Manager, DDDP, HFD-540

FDA Attendees, Titles, and Office/Division:

Jonathan Wilkin, M.D., Division Director, DDDDP, HFD-540
Wilson DeCamp, Ph.D., Team Leader, Chemistry, DNDCIII, HFD-830
Mamta Gautam-Basak, Ph.D., Chemistry Reviewer, DNDCIII, HFD-830
Barbara Hill, Ph.D., Acting Pharmacology/Toxicology Team Leader, DDDDP, HFD-540
David Allen, Pharmacology/Toxicology Reviewer, DDDDP, HFD-540
Markham Luke, M.D., Ph.D., Team Leader, DDDDP, HFD-540
Brenda Carr, M.D., Clinical Reviewer, DDDDP, HFD-540
Dennis Bashaw, Pharm.D., Team Leader, Pharmacokinetics, DPEIII, HFD-880
Mohamed Alosch, Ph.D., Biostatistics Team Leader, DBIII, HFD-725
Steve Thomson, Biostatistics Reviewer, DBIII, HFD-725
Charles J. Ganley, M.D., Division Director, DOTCDP, HFD-560
John Lipnicki, Team Leader, Microbiology, DOTCDP, HFD-560
Daiva Shetty, M.D., Clinical Reviewer, DOTCDP, HFD-560
Houda Mahayni, IDS, DOTCDP, HFD-560
Daniel Keravich, Project Manager, DOTCDP, HFD-560
Walter Ellenberg, Project Manager, DOTCDP, HFD-560
Leah Cutter, Project Manager, DOTCDP, HFD-560
Jonca Bull, M.D., Director, ODE V
Terri Rumble, BS.N, Associate Director, Regulatory Affairs, ODE V
Jacquelyn Smith, Regulatory Project Manager, DDDDP, HFD-540

External Constituent Attendees and Titles:

Vivian Chester, Vice President, Global Research and Development
Stephenie Barba, Executive Director, Regulatory Affairs
Fouad Amer, M.D., MPH, Director, Clinical Development
Raymond Dann, Director, Regulatory Affairs
Elise Olson, M.D., Consultant
Angelo Petrillo, Global Project Manger

Barbara Korbely, Global Clinical Development
David Meyers, Team Leader, Global Pharmaceutical Sciences
Robert DeWit, Director, Drug Development/Reproductive Toxicology
Richard Davison, CMC Documentation, Global Pharmaceutical Sciences
Gary Ewing, Group Leader, Pharmaceutical Sciences

Purpose:

To provide general guidance on content and format of the Investigational New Drug Application under 21 CFR 312. The briefing document submitted December 18, 2002 provides background and questions for discussion.

Chemistry, Manufacturing and Controls:

Sponsor's Question 1:

Is the proposed Stability Protocol, including the selection of tests, acceptable? Due to the fact that substantial stability data exists for minoxidil in currently marketed topical formulations, it is our intent to file with 6 months data. Is this acceptable?

Agency Response:

The proposed stability protocol per ICH Q1A guidelines is acceptable. The shelf life will be determined based on the data submitted and available during the review cycle. Stability data on batches used in the proposed phase 3 clinical studies should be provided in the IND. This should include complete specification testing, as proposed. Your proposal to submit 6 months of stability data on three batches (both at long term and accelerated storage conditions) of the proposed to-be-marketed formulation may be acceptable based on the justification provided.

Sponsor's Question 2:

A Release Testing Protocol is provided in this briefing package that describes the proposed testing for Phase 3 clinical supplies. Please comment on its acceptability, including its use as a future basis for release of commercial product.

Agency Response:

The provisional specification (Tab 1 & page 13) appear to be adequate for phase 3 studies, however the acceptance criteria of the specification for the to-be-marketed product will be further evaluated based on the data obtained during phase 3 studies. The HPLC identity test is considered non-specific for regulatory purposes (see ICH Q6A). We recommend that an identity test by IR (consistent with other minoxidil products) be added to the list of tests proposed for the investigational drug product.

Sponsor's Question 3:

Is the proposed Flammability testing protocol appropriate?

Agency Response:

Yes.

We have some additional comments based on our review of the information provided in the briefing package dated December 18, 2002.

- The quantitative composition of the *placebo* for each formulation being studied should be provided.
- It is claimed that after addition of _____ is a single-phase solution in the can. No tests (in-process or finished product testing) are proposed to substantiate this claim.
- Results of analytical testing (from the developmental studies described on page 3) should be submitted.
- The DMF references for all packaging components (described on page 9) should be submitted to the IND.
- A brief description of the non-USP (DPT) methods should be included in the IND.
- A copy of all labels and labeling to be provided to each investigator should be submitted.
- A request for categorical exclusion from submission of an EA should be included in the IND.

Pharmacology/Toxicology:

Sponsor's Question 1:

Assessment of the UV/Visible absorption spectrum of 5% MTF indicates that there is no need to conduct preclinical phototoxicity studies in addition to those previously completed on minoxidil topical solution. Do you concur?

Agency Response:

It does appear from the figures provided in the briefing document that the absorption spectra for 5% MTF (with or without the addition of _____ or sport _____) is similar to that of Minoxidil, 5% topical solution. Therefore, it appears to be acceptable for the sponsor to reference the previous phototoxicity studies completed with minoxidil topical solution.

Sponsor's Question 2:

The men's and women's 5% MTF products will both contain a fragrance (a different one in each case). Do you concur that no additional toxicology studies are needed to support the user of these fragrances? (To be addressed following FDA review of updated DMF _____)

Agency Response:

A decision regarding the adequacy of previous nonclinical studies to support the 5% MTF formulation will be contingent on a review of the additional information to be supplied for DMF _____. The sponsor should submit information on previous use of _____ Fragrance _____ and _____ Fragrance _____ at similar concentrations in other FDA-approved products as well as any available toxicological information on these fragrances (e.g. hypersensitivity, genotoxicity, reproductive and development toxicity). Alternatively, safety data generated from appropriately designed nonclinical studies with _____ Fragrance _____ and _____ Fragrance _____ as outlined in

the, "Draft Guidance for Industry: Nonclinical Studies for Development of Pharmaceutical Excipients," (<http://www.fda.gov/cder/guidance/3812dft.pdf>) may be submitted. During the End of Phase II meeting, the sponsor stated that a consultant's summary of the available safety data for the 2 fragrances would be submitted to DMF ——— The PharmTox reviewer pointed out that the basis for the consultant's findings would be reviewed. It is expected that the studies and corresponding data that were evaluated will also be submitted.

Biopharmaceutics:

There were no biopharmaceutics questions identified in the briefing document. The Agency has the following comments:

Inherent in the question related to the need for a calibrated dropper, is the opinion of the sponsor that the provided in vivo results from the two pk/biopharmaceutic trials did not show undue systemic absorption. At the present time we cannot agree with the sponsor as the results provided on pages 7,8, 11, and 12 all deal with mean data and lack measures of variability (i.e. SD or %CV). While instructive, mean data does not properly convey the risk potential for those subjects at the upper level of exposure. Prior to addressing the need for a calibrated dropper/syringe applicator the sponsor should provide the individual data upon which the mean data is based upon. After examination of this data the need/utility for a calibrated dosing device can then be addressed.

Clinical:

Sponsor's Question 1:

While the current dosing of our Rogaine topical minoxidil solutions is metered with a calibrated dropper, we propose to direct consumers to apply the foam product to "the Affected hair loss area," without quantitative measurement but with semi-quantitative guidance on the amount of foam applied, as the practice with other Rx foams applied to the scalp. Based on the rationale and proposed dosing directions, is this acceptable?

Agency Response:

Unlike some other foam products, the sponsor's product is intended for daily application(s) of a specified dose (approximately 50 mg of minoxidil) for an indefinite period; both safety and efficacy could be impacted by misapplication. The sponsor is requested to address how the amount of foam dispensed would be controlled in the absence of a meter. Also, the sponsor is requested to clarify the application procedures to the vertex i.e., how subjects would estimate the golf-ball sized amount to directly apply given that the vertex might be difficult to visualize during application.

Sponsor's Question 2:

Is a single study of this men's protocol design acceptable to support an indication for use on the vertex and/or frontal hair loss area with twice daily dosing?

Agency Response:

A) The recommended co-primary efficacy endpoints are nonvellus hair counts and subject assessment of treatment benefit. B) Generally, line extensions are based on either two clinical trials in which the new product is compared to vehicle, or a single, three-armed study in which the new product is compared to the currently-marketed product and the new vehicle. However, a single, adequate and well-controlled study in which the new product is compared to its vehicle might be acceptable in the study of androgenetic alopecia on the vertex. Two studies might be required for demonstration of efficacy in the frontal region, and a 16-week clinical trial may not be sufficiently long. It is not clear that the retrospective analysis that the Sponsor presents sufficiently establishes the safety and efficacy of use of their currently-marketed 5% MTS on the frontal region, e.g. efficacy was not assessed by the recommended criteria. Additionally, more information is needed regarding how the sponsor plans to define the "frontal" region. If the Sponsor plans to make any comparative claims to the currently-marketed product, two three-armed studies would be needed, i.e. the new product vs the currently-marketed product vs the foam vehicle (a solution vehicle arm could be included). C) A trial of 16 weeks duration is acceptable in the study of androgenetic alopecia on the vertex, if the Sponsor were to agree to include in the label a discussion of the diminution of treatment effect seen in the clinical trials with their currently-marketed 5% MTS.

Corrigendum: The Agency has long recommended hair counts as the objective measure for hair regrowth products. However, the Sponsor was advised that the Agency would consider alternative objective measures of hair regrowth, in addition to the Global Panel Review. Data to support any proposed alternative measure(s) should also be submitted.

Sponsor's Question 3:

Is a single study of the design of this women's protocol design acceptable to support once daily dosing?

Agency Response:

The pharmacokinetic (PK) study would not be considered sufficient to obviate the need for two adequate and well-controlled clinical trials in support of the proposed use in women, and 16 weeks may not be a sufficiently long duration for such trials. The safety and efficacy of once daily dosing with MTF 5% compared to twice daily dosing with MTS 2% is unclear. Clinical trials have not demonstrated that the twice daily use of the MTS 5% offers any benefit over MTS 2% twice daily in the treatment of androgenetic alopecia in women (such trials have demonstrated increased incidence of hypertrichosis with the higher concentration, however). Previous Agency advice to the Sponsor included the suggestion that a dose-ranging study be conducted, comparing the 5% foam, a 2% foam and vehicle; the Agency stands by that advice.

Information pertaining to the safety and efficacy of the MTF 5% once daily compared to the MTS 2% twice daily would be helpful. It is possible, perhaps even likely, that some consumers would gravitate towards the 5% strength, assuming it to be more effective than the lower 2% concentration. Also, the less frequent, and presumably, more convenient once daily application of the foam might sway consumers to consider switching to the 5% foam.

Additional comments:

1. No commitments can be made in the absence of sufficient information, e.g., the methodologies for the Global Panel Review, hair counts and photographic procedures were not included in the draft protocols.

2. The sponsor proposes to use different fragrances in the product planned for marketing to males and that proposed for females. The clinical trials should be conducted with the to-be-marketed formulations. Topical safety studies would be required for each to-be-marketed formulation; however, separate clinical studies for each of the to-be-marketed products may not be required (if the studies are of an appropriate design).
3. Minoxidil levels should be obtained in the face of any cardiovascular events and with hypertrichosis on sites distant from the hairline.

The Sponsor inquired whether topical safety studies with the fragranced formulations would support marketing of an unfragranced formula. Agency advises that the studies with the fragranced formulas would have to reveal no irritation or sensitization potential, in order to support marketing of an unfragranced formula. Inclusion of the unfragranced formula in a clinical study may be useful to tease out whether the fragrance was a contributing factor in any irritation or sensitization seen.

All photographs should be maintained so that they are available to the reviewer (on request).

Since the product is for cosmetic use, it is important that subject assessment of treatment benefit be assessed.

Biostatistics

There were no biostatistics questions identified in the briefing document. The Agency has the following comments:

General Comments on the Protocols:

1. As noted by the Medical Officer, for assessing effect on alopecia, both the subject self assessment and the hair count or change from baseline in hair count, should be used to assess efficacy.
2. The sponsor should power their studies based on the results of these endpoints.
3. Details of the randomization should be provided. For both administrative reasons and to balance effects across time and centers, we would recommend blocked randomization within centers (say with a blocksize between 6 and 12 or so).
4. Note that the proposed regrowth assessment seems to require an explicit reference to each subject's baseline condition by each evaluator. Because of the difficulty of adequately, comparing to baseline condition the DDDDP has generally preferred "static" measures of evaluation, where the reference is to general clinical experience not the condition of the specific subject.
5. Virtually no details of the statistical analysis are provided. The choice of hypotheses to be tested, test statistics, covariates, etc. all need to be done prior to initiating the studies. A description of possible alternative tests in case the assumptions of the original tests are not met by the resulting data should also be included. Results of post hoc analyses can not be taken in support of efficacy.

During the meeting the sponsor re-iterated their rationale of using the evaluators' assessment of hair growth as a primary endpoint instead of using difference from baseline in hair counts as

recommended by the Division. In response the Division pointed out the need to maintain consistency with other applications of using hair count and subject assessment of benefit. The sponsor, however, may pursue their proposal to the Agency by providing additional information to support the utility of using the evaluators' assessment. Among other information, the sponsor should provide information on the reliability of the evaluators' assessment and measures of their agreement when photographic data are blinded for treatment and time they were taken. It may be possible to have the new assessments as secondary endpoints with those analyses submitted to Agency for review. The Sponsor was offered a Special Protocol Assessment for Agency to further evaluate such a proposal.

Over-the-Counter Comments

The statement "~~_____~~" may confuse the consumer. Foams are tricky to reproduce. Variability in temperature and the amount and/or ratio of other inactive ingredients in the product may cause the foam to disappear at different rates. This may result in large variation of the amount applied. Variability in the amount of the drug dispensed without a metered dosing device may affect its efficacy and safety. The sponsor will need to justify why there is no need for a measuring device. The sponsor should develop a quantitative measurement device for the new product. *During the meeting the sponsor noted that they would do additional work in the area of product dosing and labeling issues so that the product can be safely used in the OTC setting.*

The comparative data from the pharmacokinetic studies suggest that the 5% foam minoxidil levels are similar to the 2% Minoxidil topical solution (MTS). Although blood levels are not a surrogate for efficacy, this data does raise some concern about the comparative efficacy of different minoxidil products. Consumers are likely to believe that 5% foam is as effective as a 5% MTS product. Therefore, the question becomes how will this new minoxidil formulation be marketed in the OTC market place. Ideally, it would be useful public health information to know the relative efficacy for this new product compared to the 5% MTS. The sponsor should consider conducting a three arm safety and efficacy trial comparing the new formulation to the already approved 5% MTS and placebo in men.

Just as the currently marketed product label has pictures describing hair loss on the vertex area of the head, the new product label should clearly describe what is meant by frontal hair loss.

The sponsor has not been able to establish a difference in efficacy for women between a 5% and 2% solution. The sponsor will need to justify why a higher concentration of foam is acceptable if they have not adequately evaluated 2% foam. For the 5% minoxidil foam formulation for women, the safety and efficacy trials should include the currently marketed 2% MTS. Since this is a new formulation, higher concentration, and a different dosing regimen, the sponsor should conduct 2 efficacy and safety trials in women.

The duration of the proposed studies in men and women seem to be too short considering long-term use of the product. For assessment of safety, the sponsor is encouraged to follow the ICH E1A document guidelines. In lieu of conducting additional studies, the sponsor will need to explain and justify how the proposed study will provide sufficient safety information with regard to local effects. Safety with respect to topical irritation and facial hair growth in women should be evaluated. *During the meeting the sponsor noted that they will have sufficient safety data on 5% minoxidil from their previous studies with 5% MTS in men and women. Agency discussed the need for consideration of the new topical formulation with regard to safety.*

Depending on the results of efficacy and safety studies, and labeling claims, the sponsor may need to conduct a label comprehension study to evaluate consumer understanding of the difference between Rogaine Extra Strength (minoxidil 5% product), Rogaine Regular Strength (the 2% product), and 5% minoxidil foam formulation with respect to expected efficacy and safety.

Administrative Comments:

1. For applications submitted after February 2, 1999, per 21CFR 54.3 and 21CFR 54.4, an NDA applicant is required either to certify to the absence of certain financial interests of clinical investigators or disclose those financial interests.
2. The Sponsor is encouraged to submit the full text protocol to the IND as Special Protocol through the 45-day Special Protocol Assessment (SPA) mechanism for Agency review, comment and agreement, prior to study initiation.
3. Comments shared today with the Sponsor are based upon the contents of the briefing document, which is considered to be an informational aid to facilitate today's discussion. Review of the information submitted to the IND might identify additional comments or informational requests.

Minutes Preparer: _____
Jacquelyn Smith/Regulatory Project Manager, DDDP, HFD-540

Chair Concurrence: _____
Jonathan Wilkin, M.D./Division Director, DDDDP, HFD-540

Appears This Way
On Original

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

/s/

John Kelsey
3/24/03 01:39:05 PM
for Dr. Wilkin

Appears This Way
On Original

REGULATORY AFFAIRS
Received

DEPARTMENT OF HEALTH & HUMAN SERVICES AUG 31 2000

NDA 20-834

Food and Drug Administration
Rockville MD 20857

Pharmacia & Upjohn Company
Attention: Raymond E. Dann, Ph.D.
Director, Regulatory Affairs
100 Route 206 North
Peapack, New Jersey 07977

AUG 31 2000

Dear Dr. Dann:

Reference is made to your correspondence dated July 25, 2000, requesting FDA issue a Written Request under Section 505A of the Food, Drug, and Cosmetic Act for Rogaine (minoxidil topical solution) 5%, Extra Strength for Men.

Please also refer to our telephone conference on August 29, 2000, which included Dr. Robert J. DeLap, Dr. Markham Luke, Dr. Lisa Mathis, Dr. Dennis Bashaw, Mary Jean Kozma Fornaro, and myself to discuss this submission. We have reviewed your proposed pediatric study request and are unable to issue a Written Request based on your submission. Your suggested proposal would not provide any additional needed data to adequately label the product for use in the pediatric population 15 years of age and older, because the clinical studies in adults are sufficient to label the product for this relevant pediatric population, if there is evidence of a population of 15 to 17 year olds with sufficient vertex androgenetic alopecia to seek medical care. We recommend you submit a labeling supplement to reflect that the product is labeled for patients 15 years old and above.

We look forward to working with you in your endeavors to develop additional pediatric information that may produce health benefits to the pediatric population. If you have any questions, contact Mary Jean Kozma-Fornaro, Supervisor, Project Management Staff, at 301 827-2020.

Sincerely,



Jonathan K. Wilkin, M.D.

Director

Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research