**CENTER FOR DRUG EVALUATION AND RESEARCH**

# Approval Package for:

***APPLICATION NUMBER:***

# ANDA 075737

**Name:** Minoxidil Topical Solution USP, 5%

**Sponsor:** Clay-Park Labs, Inc.

**Approval Date:** March 15, 2002

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

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# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# APPROVAL LETTER

ANDA 75-737

MAR 15 2002

Clay-Park Labs, Inc.
Attention: Candis Edwards
1700 Bathgate Ave.
Bronx, NY 10457

Dear Madam:

This is in reference to your abbreviated new drug application dated November 18, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Minoxidil Topical Solution USP, 5% (For Men).

Reference is also made to your amendments dated September 6, and December 6, 2001.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted Over-The-Counter (OTC) labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Minoxidil Topical Solution USP, 5% (For Men) to be bioequivalent to the listed drug (Rogaine® Extra Strength, 5% (For Men) of Pharmacia & Upjohn Co.).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

Robert Lee Seth for 3/15/2002

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-737
Division File
Field Copy
HFD-610/R. West
HFD-210/B. Poole
HFD-330
HFD-205

Endorsements:
HFD-623/N.Takiar/ N-Takiar 3/6/02
HFD-623/D.Gill/ DSGill 3-7-02
HFD-617/R.Wu BWu 3/7/02
HFD-613/L.Golson/ LG Golson 3/7/02
HFD-613/J.Grace/ John Grace 3/7/2002

Robert West 3/15/02

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F/T by: DJ 3/6/02

APPROVAL

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# LABELING

# Minoxidil Topical Solution USP, 5% Extra Strength For Men

APPROVED MAR 15 2002

- Provides more hair regrowth than Minoxidil Topical Solution, 2% For Men.
- Results may occur at 2 months with twice daily usage. For some men, it may take at least 4 months for results to be seen.

Please read this leaflet carefully. It will help you understand how to use Minoxidil Topical Solution, 5% and what to expect from its use. If you have any questions after reading this leaflet, or anytime while using Minoxidil Topical Solution, 5% you should ask your health care professional.

**What is Minoxidil Topical Solution, 5%?**
Minoxidil Topical Solution, 5% is a colorless liquid medication containing 5% minoxidil for use only on the scalp to help regrow hair in men.

**Who may use Minoxidil Topical Solution, 5%?**
Minoxidil Topical Solution, 5% is for use only by men. Minoxidil Topical Solution, 5% may be appropriate for you if you are a male at least 18 years old and experiencing gradually thinning hair or gradual hair loss on the top of the scalp ( vertex only, as shown on the side panel of the box). It is not intended for frontal baldness or a receding hairline. The common inherited thinning or hair loss process begins slowly and may become noticeable only after years of gradual loss. Minoxidil Topical Solution, 5% is for men with hair loss or thinning hair that begins on the vertex of the scalp. Minoxidil Topical Solution, 5% is more likely to regrow hair in men with hair loss in the range shown on the side panel of the box. If men have more hair loss than shown on the side panel of the box, Minoxidil Topical Solution, 5% may not work. Many of those experiencing hair loss have other family members with gradual thinning hair or hair loss. **If you have no family history of gradual thinning hair or of gradual hair loss, or your hair loss is patchy, see your doctor.**

**Who should NOT use Minoxidil Topical Solution, 5%?**

- Women should not use Minoxidil Topical Solution, 5% because studies have shown it works no better in woman than Minoxidil for Women. Some women may also grow facial hair. In addition, Minoxidil Topical Solution, 5% may be harmful if used during pregnancy or breast-feeding.
- Minoxidil Topical Solution, 5% should not be used on babies or for children under 18 years old.
- Minoxidil Topical Solution, 5% will not prevent or improve hair loss which may occur with the use of some prescription and non-prescription medications, certain severe nutritional problems (very low body iron; too much vitamin A intake), low thyroid states (hypothyroidism), chemotherapy, or diseases which cause scarring of the scalp. Also, Minoxidil Topical Solution, 5% will not improve hair loss due to:
  - damage from the use of hair care products which cause scarring or deep burns of the scalp.
  - hair grooming methods such as cornrowing or ponytails which require pulling the hair tightly back from the scalp.

**Do not use if you are not sure of the reason for your hair loss.**

**Minoxidil Topical Solution, 5% For Men differs from Minoxidil Topical Solution, 2% For Men products in the following ways:**

- Contains 5% Minoxidil (Minoxidil Regular Strength contains 2%).
- Regrows more hair.
- With Minoxidil Topical Solution, 5% For Men, results may occur at 2 months with twice daily use. For some men, it may take at least 4 months for results to be seen.
- Is more likely to cause scalp irritation. If scalp irritation continues or worsens, stop use and see a doctor. See Warnings on carton or bottle label.

**Will Minoxidil Topical Solution, 5% work for me?**
The amount of hair regrowth is different for each person. Not everyone will respond to Minoxidil Topical Solution, 5%. The response to Minoxidil Topical Solution, 5% cannot be predicted. It is unlikely anyone will be able to grow back all their hair. However, to see your best results with Minoxidil Topical Solution, 5%, make sure you get the medicine directly to the scalp and apply it twice a day everyday. You may get better results if you have been losing your hair for a short period of time or have little hair loss. However, for some men Minoxidil Topical Solution, 5% may not work.

**How soon can I expect results from using Minoxidil Topical Solution, 5%?**
Since normal hair usually grows only 1/2 to 1 inch per month, hair regrowth with Minoxidil Topical Solution, 5% also takes time. Results may be seen as early as 2 months with twice daily use. For some men, it may take at least 4 months for results to be seen. If you do not see *any* results after 4 months, stop using Minoxidil Topical Solution, 5%. When you **first** begin to use Minoxidil Topical Solution, 5%, your hair loss may increase temporarily for up to 2 weeks. This is likely a sign that you are getting rid of old hairs in order to regrow more new hairs. This temporary increase in hair loss is expected and is a part of the process for how Minoxidil Topical Solution, 5% regrows hair. Remember, this increased hair loss is temporary. However, if it continues after two weeks, see your doctor.

**If Minoxidil Topical Solution, 5% is working, what will the hair look like?**
At first, hair growth is usually soft, downy, colorless hairs (like peach fuzz). After further use, the new hairs should be the same color and thickness as the other hairs on your scalp.

**How long do I need to use Minoxidil Topical Solution, 5%?**
If you experience hair regrowth, continued use of Minoxidil Topical Solution, 5% is necessary or the hair loss will begin again. In studies with Minoxidil Topical Solution, 5% For Men, hair regrowth has not been shown to last longer than 48 weeks of continuous treatment in large clinical trials.

**What happens if I completely stop using Minoxidil Topical Solution, 5%? Will I keep the new hair?**
Continuous use of Minoxidil Topical Solution, 5% is needed to maintain hair regrowth. If you stop using Minoxidil Topical Solution, 5%, you will lose your newly regrown hair in 3 to 4 months.

**How do I use Minoxidil Topical Solution, 5%?**
For best results, apply 1 mL with dropper or sprayer (6 sprays) **2 times a day directly onto the scalp** in the hair loss area. Using more or using more often will not improve results. Each bottle should last about 25-30 days, if used as directed.
It is not necessary to use fingertips when applying Minoxidil Topical Solution, 5%. However, if you do use your fingertips, wash your hands well immediately afterwards. Allow time for Minoxidil Topical Solution, 5% to dry completely before wearing a hat, or lying on a pillow, etc. Minoxidil Topical Solution, 5% may cause staining of clothing or linens if damp on the scalp. When applying Minoxidil Topical Solution, 5% at night, be sure to allow 2 to 4 hours to dry completely. Never take this product by mouth or apply to other parts of the body.

**When do I use Minoxidil Topical Solution, 5%?**
Apply Minoxidil Topical Solution, 5% once in the morning and once at night. The nighttime application should occur 2 to 4 hours before going to bed to allow for drying. Each bottle should last about 25-30 days, if used as directed.

**What if I miss a dose or forget to use Minoxidil Topical Solution, 5%?**
If you miss one or two daily doses of Minoxidil Topical Solution, 5%, just continue with your next dose. You should not make up for missed doses.

**Can I use Minoxidil Topical Solution, 5% more than twice a day? Will it work faster, better?**
No. Minoxidil Topical Solution, 5% will not work faster or better if used more than two times a day. Studies have been carefully conducted to determine the correct amount of Minoxidil Topical Solution, 5% needed to get the best results. More frequent use or larger doses have not been shown to speed up hair growth and may increase your chance of side effects.

**What kind of shampoo should I use with Minoxidil Topical Solution, 5%?**
If you wash your scalp before applying Minoxidil Topical Solution, 5%, use a mild shampoo.

**Can I use hair sprays, mousses, conditioners, gels, etc.?**
Hair sprays, spritz, or styling aids may be used on your hair while using Minoxidil Topical Solution, 5%. For best results, Minoxidil Topical Solution, 5% should be allowed to soak into scalp before using any styling products.Try to develop a good routine of applying Minoxidil Topical Solution, 5% first, and then applying styling products and style as usual. Keep in mind that your best results will be seen with proper application.

**Can I have my hair colored or permed or use hair relaxers while using Minoxidil Topical Solution, 5%?**
We have no evidence that coloring or perming your hair or that the use of relaxers change the effect of Minoxidil Topical Solution, 5%. However, because the use of a permanent wave and hair color can cause scalp irritation on certain people, we recommend the following precautions:
1) To avoid possible scalp irritation, you should make sure all of the Minoxidil Topical Solution, 5% has been washed off the hair and scalp before using color or perm chemicals.
2) For best results, do not apply Minoxidil Topical Solution, 5% on the same day that you use a chemical treatment on your hair.
3) Do not use Minoxidil Topical Solution, 5% for 24 hours after using any chemicals to make sure your scalp has not been irritated by the perm or color treatment. If no irritation occurs, continue use of Minoxidil Topical Solution, 5% as usual.
4) Simply restart your normal Minoxidil Topical Solution, 5% routine. There is no need to use more Minoxidil Topical Solution, 5% to make up for missed applications. Missing one day of Minoxidil Topical Solution, 5% will not affect your hair regrowth results.

**Can I apply Minoxidil Topical Solution, 5% and wash my hair an hour later?**
No. For Minoxidil Topical Solution, 5% to work best, you should allow it to stay on the scalp for about 4 hours before washing.

**How to use the Applicators**
**Applicator Options**
**See pictures on the side panel of the carton**
We have included two applicators that have been designed especially for men. You can choose whichever one works best for you.

A. Dropper
The child-resistant dropper can be useful for a broad range of hair styles or hair loss because it allows for easy application through the hair and directly onto the scalp.

B. Sprayer
The sprayer may be more useful for larger areas of hair loss.

**Using the Applicators**
***Important:*** When applying Minoxidil Topical Solution, 5%, make sure the medicine comes in direct contact with the scalp. The medicine will not work if it is sprayed only on your hair and does not reach your scalp.

A. Dropper
1. Squeeze the rubber bulb and put the dropper into the bottle. Release the bulb, allowing the dropper to fill to the 1 mL line. If the level of medicine is above the 1 mL line, squeeze the extra amount back into the bottle.
2. Next, place the tip of the dropper near the part of the scalp you want to treat and gently squeeze the bulb to release the medicine gradually. To prevent the medicine from running off the scalp, apply a small amount at a time.

B. Sprayer
**The spray (B) applicator is NOT child-resistant. If you have small children, keep the original child-resistant cap and place it back on the bottle after each use.**
1. Put the spray applicator into the bottle and twist it on firmly.
2. Next, holding the bottle upright, pump the spray attachment 6 times to get one full dose (1 mL). Be careful not to inhale the mist.

**Do not use Minoxidil Topical Solution, 5% if you are:**

- a woman
- not sure of the reason for your hair loss
- under 18 years of age. Not for babies and children.
- using other medicines on the scalp

**Do not use if you have:**

- no family history of hair loss
- sudden and/or patchy hair loss
- a red, inflamed, infected, irritated or painful scalp

**Not For Use By Women:** May grow facial hair. May be harmful if used during pregnancy or breast-feeding

**Stop use and see a doctor if you get:**

- chest pain, a rapid heartbeat, faintness or dizziness
- sudden, unexplained weight gain
- swollen hands or feet
- scalp irritation that continues or worsens

For external use only.
Avoid contact with eyes. In case of accidental contact, rinse with large amounts of cool tap water.

**Keep this and all drugs out of the reach of children.** Do not use on babies or children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

**What are the most common side effects with Minoxidil Topical Solution, 5%?**
The most common side effects are itching and skin irritation of the treated area of the scalp. If scalp irritation continues, stop use and see a doctor. Minoxidil Topical Solution, 5% contains alcohol, which will cause burning or irritation of the eyes. If Minoxidil Topical Solution, 5% accidentally gets into eyes, rinse with large amounts of cool tap water.

**Can Minoxidil Topical Solution, 5% produce unwanted hair growth?**
Unwanted hair growth on the face and other parts of the body has been reported in women. But it is rare and reversible. If you develop unwanted hair, stop using Minoxidil Topical Solution, 5%. Over time, the unwanted hair, if caused by Minoxidil Topical Solution, 5%, will go away. You can take the following steps to decrease the chances of unwanted hair growth:
1) limit the application of Minoxidil Topical Solution, 5% only to the scalp;
2) if you use your hands to apply Minoxidil Topical Solution, 5%, wash your hands well immediately afterwards; and 3) after your nighttime application of Minoxidil Topical Solution, 5%, allow enough drying time before going to bed (usually 2 to 4 hours).

**Can I use Minoxidil Topical Solution, 5% for baldness or hair loss in babies or children?**
No. Minoxidil Topical Solution, 5% must not be used to treat baldness or hair loss in babies and children.

If you have any other questions, ask your health care professional.
**Store at Controlled Room Temperature 20° to 25° C (68° to 77° F). Keep tightly closed.**

Mfg. By:
**CLAY-PARK LABS, INC.**
Bronx, NY 10457

039-1

70%

## MINOXIDIL TOPICAL SOLUTION USP, 5% FOR MEN

**Active Ingredient:** Minoxidil 5% w/v

**Purpose:** Hair Regrowth Treatment For Men.

**Use :**
- To regrow hair on top of the scalp (vertex only, see pictures on side of carton). Not intended for frontal baldness or receding hairline.
- It takes time to regrow hair. With Minoxidil Topical Solution USP, 5% For Men, results may occur at 2 months with twice daily usage. For some men, it may take at least 4 months for results to be seen.
- The amount of hair regrowth is different for each person. Minoxidil Topical Solution USP, 5% For Men will not work for all men.
- Clinical research in mostly white men aged 18-49 years with moderate degrees of hair loss showed that Minoxidil Topical Solution USP, 5% For Men provides more hair regrowth than regular strength Minoxidil Topical Solution, 2% For Men.
- If your amount of hair loss is more than that shown on the side of this carton, or your hair loss is on the front of the scalp, Minoxidil Topical Solution USP, 5% For Men may not work.
- Continued use is necessary or hair loss will begin again. If you do not see hair regrowth in 4 months, stop use. In studies with Minoxidil Topical Solution USP, 5% For Men, hair regrowth has not been shown to last longer than 48 weeks of continuous treatment in large clinical trials.

**Warnings:**

**Do Not Use If You Are:**
- a women
- not sure of the reason for your hair loss
- under 18 years of age. Not for babies or children.
- using other medicines on the scalp

**Not For Use By Women:**
May grow facial hair.
May be harmful if used during pregnancy or breast-feeding.

**Do Not Use If You Have:**
- no family history of hair loss
- sudden and/or patchy hair loss
- a red, inflamed, infected, irritated or painful scalp

MAR 15 2002

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**Stop Use and See A Doctor If You Get:**
- chest pain, a rapid heartbeat, faintness, or dizziness
- sudden, unexplained weight gain
- swollen hands or feet
- scalp irritation that continues or worsens

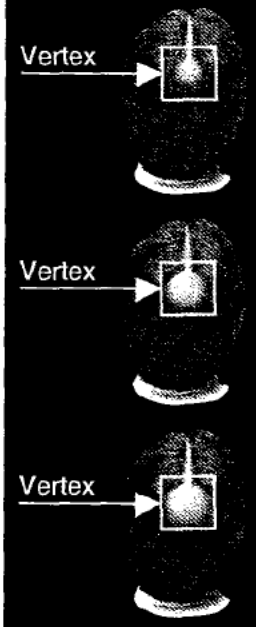
For external use only.
Avoid contact with eyes. In case of accidental contact, rinse with large amounts of cool tap water.
**Keep this and all drugs out of the reach of children.** Do not use on babies or children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

Keep the carton and educational booklet. They contain important information.

**Directions:** For external use only. **For use by men only.** Apply 1 mL with dropper or sprayer (6 sprays) **2 times a day directly onto the scalp** in the hair loss area.
Using more, or using more often will not improve results. Do not apply on other parts of the body.

UPC
0-81642-21846

Minoxidil Topical Solution USP, 5% is for men who have a general thinning of hair on the top of the scalp (vertex only, as shown below). Not intended for frontal baldness or a receding hairline. Minoxidil Topical Solution USP, 5% For Men has been shown to regrow hair in men with the following degrees of thinning hair or hair loss.




If men have more hair loss or hair loss in a place different than shown above, Minoxidil Topical Solution USP, 5% For Men may not work.

# MINOXIDIL TOPICAL SOLUTION USP, 5%

HAIR REGROWTH TREATMENT
Extra Strength For Men
(Read enclosed booklet before use)

NDC 45802-218-46

# MINOXIDIL TOPICAL SOLUTION USP, 5%

## HAIR REGROWTH TREATMENT
## Extra Strength For Men

## Regrows More Hair Results May Occur at 2 Months

Not For Use By Women

60 mL (2 FL OZ)

026-7

NOXIDIL
PICAL SOLUTION
P, 5%
REGROWTH TREATMENT
Strength For Men
closed booklet before use)

45802-218-46

NOXIDIL
OPICAL SOLUTION
SP, 5%
R REGROWTH TREATMENT
a Strength For Men

grows More Hair
ults May Occur
2 Months

Not For Use
By Women

60 mL (2 FL OZ)

2182CPL-3
N0101

Inactive ingredients:
Alcohol, 30% v/v, propylene glycol, 50% v/v, and purified water.

This package contains:
One 60 mL (2 FL OZ) Bottle of MINOXIDIL TOPICAL SOLUTION USP, 5% For Men (lasts about 25 – 30 days).
One child-resistant dropper applicator
One sprayer applicator (not child-resistant)


One 60 mL (2 FL OZ) Bottle of Extra Strength Minoxidil Topical Solution USP, 5% (lasts about 25 – 30 days).

One child-resistant dropper applicator

One sprayer applicator (not child-resistant)

This package also includes an educational booklet.

Store at Controlled Room Temperature 20° to 25° C (68° to 77° F). Keep tightly closed. Lot No. & Exp. Date see label or see box.

Mfg. By:
**CLAY-PARK LABS, INC.**
Bronx, NY 10457

Clay Park Labs,Inc. Graphics Dept. (Ph 718 960-9967)

| | | |
|---|---|---|
| DIE# 20877 | (b) (4) | PRODUCT NO: 218 |
| CODE# 54 | | MAC ARTIST: (b) (6) |

For external use only.
Avoid contact with eyes. In case of accidental contact, rinse with large amounts of cool tap water.
**Keep this and all drugs out of the reach of children.** Do not use on babies or children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

See carton or educational leaflet for additional information.

Each mL contains: Minoxidil 5% w/v, alcohol, 30% v/v, propylene glycol, 50% v/v, and purified water.

**Not For Use By Women:**
May grow facial hair.
May be harmful if used during pregnancy or breast-feeding.

**Store at Controlled Room Temperature 20° to 25° C (68° to 77° F). Keep tightly closed. Lot No. & Exp. Date see label or see box.**
Mfg. By:
**CLAY-PARK LABS, INC.**
Bronx, NY 10457

NDC 45802-218-46

# Minoxidil Topical Solution USP, 5%

HAIR REGROWTH TREATMENT
Extra Strength For Men

For external use only
Do not use if you are under 18 years of age.

60 mL (2 FL OZ)

**Directions:** For external use only.
**For use by men only.** Apply 1 mL with dropper or sprayer (6 sprays) **2 times a day directly onto the scalp** in the hair loss area. Using more or using more often will not improve results. Do not apply on other parts of the body.

APPROVED
MAR 2002

**Warnings**
**Do not use if you are:**
- a woman
- not sure of the reason for your hair loss
- under 18 years of age. Not for babies or children.
- using other medicines on the scalp

**Do not use if you have:**
- no family history of hair loss
- sudden and/or patchy hair loss
- a red, inflamed, infected, irritated or painful scalp

**Stop use and ask a doctor if you get:**
- chest pain, a rapid heartbeat, faintness or dizziness
- sudden, unexplained weight gain
- swollen hands or feet
- scalp irritation that continues or worsens

LCPL21846-3 N0500

2-995

**LABEL SIZE**
**4 X 2.5**

(b) (4)

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# LABELING REVIEWS

**REVIEW OF PROFESSIONAL LABELING**
**DIVISION OF LABELING AND PROGRAM SUPPORT**
**LABELING REVIEW BRANCH**

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ANDA Number: 75-737 Date of Submission: November 19, 1999

Applicant's Name: Clay-Park Labs, Inc.

Established Name: Minoxidil Topical Solution USP, 5%

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Labeling Deficiencies:

1. GENERAL COMMENTS

   a. Please revise your labeling to use the established name of this product, "Minoxidil Topical Solution", rather than [redacted] (b) (4) Minoxidil Topical Solution" along with the product's strength.

   b. We recommend that you only use "USP" with the established name and strength on the container label, carton labeling and in the insert title.

   c. Include "Keep tightly closed" with your storage recommendation.

   d. Please refer to 16 CFR 1700.14(a)(28) regarding "Requirements for Child-Resistant Packaging; Minoxidil Preparations With More Than 14 mg of Minoxidil Per Package" and advise the Agency of your plans.

2. CONTAINER (60 mL)

   a. Principal Display Panel

      21 CFR 201.61 requires a statement of identity, consisting of the established name followed by the pharmacological category, appear on the principal display panel of an over-the-counter drug package. The statement "Extra Strength for Men" should appear separate, of different prominence from, and follow the statement of identity. We recommend the following:

      **MINOXIDIL TOPICAL SOLUTION, 5%**

      HAIR REGROWTH TREATMENT

      Extra Strength for Men

   b. The [redacted] (b) (4) used for the text appearing below the established name and strength is too dark and does not offer a great enough contrast to be easily seen and read. Please revise to use something easier seen against a black background.

3. CARTON (1 x 60 mL)

   a. See GENERAL COMMENTS.

   b. See CONTAINER COMMENTS.

4. PATIENT BOOKLET

   a. See GENERAL COMMENTS.

B. How to Use the Applicators (Applicator Options – Sprayer)

Include "See pictures on the side panel of the carton" as the ultimate sentence.

Please revise your labels and labeling, as instructed above, and submit in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference-listed drug. We suggest that you routinely monitor the following web site for any approved changes –

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

## REVIEW OF PROFESSIONAL LABELING CHECK LIST

| Established Name | Yes | No | N.A. |
|---|---|---|---|
| Different name than on acceptance to file letter? | | X | |
| Is this product a USP item? If so, USP supplement in which verification was assured. USP 24 | X | | |
| Is this name different than that used in the Orange Book? | | X | |
| If not USP, has the product name been proposed in the PF? | | | X |
| **Error Prevention Analysis** | | | |
| Has the firm proposed a proprietary name? If yes, complete this subsection. | | X | |
| Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? | | | X |
| Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? | | | X |
| **Packaging** | | | |
| Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. | | X | |
| Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. | X | | |
| Does the package proposed have any safety and/or regulatory concerns? | X | | |
| If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection? | | | X |
| Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration? | | X | |
| Is the strength and/or concentration of the product unsupported by the insert labeling? | | X | |
| Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? | | | X |
| Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? | | X | |
| Are there any other safety concerns? | | X | |
| **Labeling** | | | |
| Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label). | | X | |
| Has applicant failed to clearly differentiate multiple product strengths? | | | X |
| Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines) | | X | |
| **Labeling(continued)** | **Yes** | **No** | **N.A.** |
| Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA) | X | | |
| Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed? | | X | |
| Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED? | | | X |
| Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported. | | | |
| Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR | | | |

| | | | |
|---|---|---|---|
| Is the scoring configuration different than the RLD? | | | X |
| Has the firm failed to describe the scoring in the HOW SUPPLIED section? | | | X |
| Inactive Ingredients: (FTR: List page # in application where inactives are listed) | | | |
| Does the product contain alcohol? If so, has the accuracy of the statement been confirmed? | X | | |
| Do any of the inactives differ in concentration for this route of administration? | | X | |
| Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)? | | | |
| Is there a discrepancy in inactives between DESCRIPTION and the composition statement? | | X | |
| Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported? | | X | |
| Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? | | | X |
| Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION? | | | X |
| Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed) | | | X |
| USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations) | | | |
| Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable? | | X | |
| Does USP have labeling recommendations? If any, does ANDA meet them? | | X | |
| Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? | | X | |
| Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. | | | |
| Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) | | | |
| Insert labeling references a food effect or a no-effect? If so, was a food study done? | | X | |
| Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why. | | X | |
| Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. | | | |

**NOTES/QUESTIONS TO THE CHEMIST:**

1. **The labeling states that there is 30% alcohol (v/v) in this product. Is this accurate?**

2. **Please verify that 6 sprays deliver 1 mL of solution.**

3. **Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At the time the rule was passed, such closures were not yet available. However, firms must comply once they do become available. Clay-Park has been asked to advise the Agency on their plans concerning this matter.**

---

**FOR THE RECORD:**

1. **Labeling review based on the labeling for Rogaine Extra Strength for Men, 5% (NDA 20-834) – Pharmacia and Upjohn Consumer Healthcare; approved November 14, 1997.**

2. **Packaging**
   **Rogaine packages its extra strength product in 1 x 60 mL and 2 x 60 mL cartons.**

Clay-Park is proposing to package its white, HDPE 60 mL bottles in cartons of one. The primary closure and the dropper are child resistant. The sprayer is not.

Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At present, the sprayer is not child-resistant (see 16 CFR 1700.14(a)(28). At the time this rule was passed, child resistant closures for the sprayers were not yet available. However, firms must advise the Agency of their plans and comply once such closures do become available.

3. Labeling
Although the innovator calls its product "Rogaine Extra Strength for Men", the applicant has been asked to revise its labeling to use just the established name.

4. Inactive Ingredients
There does not appear to be discrepancies between the labeling and the C&C Statements.

5. USP Issues
USP – Preserve in tight containers
RLD – Store at CRT, 20-25°C (68-77°F).
ANDA – Store at CRT, 20-25°C (68-77°F). Clay-Park has been asked to include "Keep tightly closed" with its storage recommendation.

6. Bio Issues – Waiver granted 1/21/00.

7. Patents/Exclusivities – This product has marketing exclusivity protection until November 14, 2000.

---

**Date of Review:**

April 17, 2000

**Date of Submission:**

November 18, 1999

**Primary Reviewer:**

L.O. Golson

**Date:**

4/17/00

**Team Leader:**

John D. Grace

**Date:**

4/26-2000

cc:

ANDA: 75-737
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
V:\FIRMSAM\CLAYPARK\LTRS&REV\75737na1.l
Review

**REVIEW OF PROFESSIONAL LABELING**
**DIVISION OF LABELING AND PROGRAM SUPPORT**
**LABELING REVIEW BRANCH**

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ANDA Number: 75-737 Date of Submission: August 2, 2000 (Amendment)

Applicant's Name: Clay-Park Labs, Inc.

Established Name: Minoxidil Topical Solution USP, 5%

---

Labeling Deficiencies:

CARTON (1 x 60 mL)

1. The "Drug Facts" labeling format proposed for OTC products has not been approved for Rogaine® Extra Strength for Men. Please revise your carton labeling and resubmit in final print to be in accord with labeling currently approved for Rogaine.

2. Revise the ultimate sentence of the text on the side panel containing the pictorials of the degrees of baldness to read, ...following degrees of thinning hair or hair loss.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference-listed drug. We suggest that you routinely monitor the following web site for any approved changes –

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

## REVIEW OF PROFESSIONAL LABELING CHECK LIST

| Established Name | Yes | No | N.A. |
|---|---|---|---|
| Different name than on acceptance to file letter? | | X | |
| Is this product a USP item? If so, USP supplement in which verification was assured. USP 24 | X | | |
| Is this name different than that used in the Orange Book? | | X | |
| If not USP, has the product name been proposed in the PF? | | | X |
| **Error Prevention Analysis** | | | |
| Has the firm proposed a proprietary name? If yes, complete this subsection. | | X | |
| Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? | | | X |
| Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? | | | X |
| **Packaging** | | | |
| Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. | | X | |
| Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. | X | | |
| Does the package proposed have any safety and/or regulatory concerns? | X | | |
| If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection? | | | X |
| Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration? | | X | |
| Is the strength and/or concentration of the product unsupported by the insert labeling? | | X | |
| Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? | | | X |
| Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? | | X | |
| Are there any other safety concerns? | | X | |
| **Labeling** | | | |
| Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label). | | X | |
| Has applicant failed to clearly differentiate multiple product strengths? | | | X |
| Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines) | | X | |
| **Labeling(continued)** | **Yes** | **No** | **N.A.** |
| Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA) | X | | |
| Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed? | | X | |
| Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED? | | | X |
| Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported. | | | |
| **Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR** | | | |

| | | | |
|---|---|---|---|
| Is the scoring configuration different than the RLD? | | | X |
| Has the firm failed to describe the scoring in the HOW SUPPLIED section? | | | X |
| Inactive Ingredients: (FTR: List page # in application where inactives are listed) | | | |
| Does the product contain alcohol? If so, has the accuracy of the statement been confirmed? | X | | |
| Do any of the inactives differ in concentration for this route of administration? | | X | |
| Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)? | | | |
| Is there a discrepancy in inactives between DESCRIPTION and the composition statement? | | X | |
| Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported? | | X | |
| Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? | | | X |
| Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION? | | | X |
| Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed) | | | X |
| USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations) | | | |
| Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable? | | X | |
| Does USP have labeling recommendations? If any, does ANDA meet them? | | X | |
| Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? | | X | |
| Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. | | | |
| Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) | | | |
| Insert labeling references a food effect or a no-effect? If so, was a food study done? | | X | |
| Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why. | | X | |
| Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. | | | |

**NOTES/QUESTIONS TO THE CHEMIST:**

1. **The labeling states that there is 30% alcohol (v/v) in this product. Is this accurate?**

2. **Please verify that 6 sprays deliver 1 mL of solution.**

3. **Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At the time the rule was passed, such closures were not yet available. However, firms must comply once they do become available. Clay-Park has been asked to advise the Agency on their plans concerning this matter.**

---

**FOR THE RECORD:**

1. **Labeling review based on the labeling for Rogaine Extra Strength for Men, 5% (NDA 20-834) – Pharmacia and Upjohn Consumer Healthcare; approved November 14, 1997.**

2. **Packaging**
   **Rogaine packages its extra strength product in 1 x 60 mL and 2 x 60 mL cartons.**

**Clay-Park is proposing to package its white, HDPE 60 mL bottles in cartons of one. The primary closure and the dropper are child resistant. The sprayer is not.**

**Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At present, the sprayer is not child-resistant (see 16 CFR 1700.14(a)(28). At the time this rule was passed, child resistant closures for the sprayers were not yet available. However, firms must advise the Agency of their plans and comply once such closures do become available.**

3. **Labeling**
   **Although the innovator calls its product "Rogaine Extra Strength for Men", the applicant has been asked to revise its labeling to use just the established name.**

4. **Inactive Ingredients**
   **There does not appear to be discrepancies between the labeling and the C&C Statements.**

5. **USP Issues**
   **USP – Preserve in tight containers**
   **RLD – Store at CRT, 20-25°C (68-77°F).**
   **ANDA – Store at CRT, 20-25°C (68-77°F). Clay-Park has been asked to include "Keep tightly closed" with its storage recommendation.**

6. **Bio Issues – Waiver granted 1/21/00.**

7. **Patents/Exclusivities – None pending.**

---

**Date of Review:**

**January 2, 2001**

**Date of Submission:**

**August 2, 2000 (Amendment)**

**Primary Reviewer:**

Gillian N Barnes

**Date:**

1/02/01

**Team Leader:**

John L. Grace

**Date:**

1-9-2001

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cc:

ANDA: 75-737
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
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Review

**APPROVAL SUMMARY**

**REVIEW OF PROFESSIONAL LABELING**
**DIVISION OF LABELING AND PROGRAM SUPPORT**
**LABELING REVIEW BRANCH**

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ANDA Number: 75-737 Date of Submission: January 23, 2001 (Amendment)

Applicant's Name: Clay-Park Labs, Inc.

Established Name: Minoxidil Topical Solution USP, 5%

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**APPROVAL SUMMARY** (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (60 mL) – Satisfactory as of August 2, 2000 submission

Carton Labeling: (1 x 60 mL) – Satisfactory as of January 23, 2001 submission

Patient Information Sheet – Satisfactory as of August 2, 2000 submission

**BASIS OF APPROVAL:**

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Rogaine Extra Strength for Men

NDA Number: 20-834

NDA Drug Name: Minoxidil Topical Solution, 5% (For Men)

NDA Firm: Pharmacia and Upjohn Consumer Healthcare

Date of Approval of NDA Insert : November 14, 1997

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: Side-by-side comparison

Basis of Approval for the Carton Labeling: Side-by-side comparison

## REVIEW OF PROFESSIONAL LABELING CHECK LIST

| Established Name | Yes | No | N.A. |
|---|---|---|---|
| Different name than on acceptance to file letter? | | X | |
| Is this product a USP item? If so, USP supplement in which verification was assured. USP 24 | X | | |
| Is this name different than that used in the Orange Book? | | X | |
| If not USP, has the product name been proposed in the PF? | | | X |
| **Error Prevention Analysis** | | | |
| Has the firm proposed a proprietary name? If yes, complete this subsection. | | X | |
| Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? | | | X |
| Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified? | | | X |
| **Packaging** | | | |
| Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR. | | X | |
| Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. | | X | |
| Does the package proposed have any safety and/or regulatory concerns? | X | | |
| If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection? | | | X |
| Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration? | | X | |
| Is the strength and/or concentration of the product unsupported by the insert labeling? | | X | |
| Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect? | | | X |
| Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? | | X | |
| Are there any other safety concerns? | | X | |
| **Labeling** | | | |
| Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label). | | X | |
| Has applicant failed to clearly differentiate multiple product strengths? | | | X |
| Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines) | | X | |
| **Labeling(continued)** | **Yes** | **No** | **N.A.** |
| Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA) | X | | |
| Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed? | | X | |

| | | | |
|---|---|---|---|
| Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED? | | | X |
| Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported. | | | |
| Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR | | | |
| Is the scoring configuration different than the RLD? | | | X |
| Has the firm failed to describe the scoring in the HOW SUPPLIED section? | | | X |
| Inactive Ingredients: (FTR: List page # in application where inactives are listed) | | | |
| Does the product contain alcohol? If so, has the accuracy of the statement been confirmed? | X | | |
| Do any of the inactives differ in concentration for this route of administration? | | X | |
| Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)? | | | |
| Is there a discrepancy in inactives between DESCRIPTION and the composition statement? | | X | |
| Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported? | | X | |
| Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? | | | X |
| Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION? | | | X |
| Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed) | | | X |
| USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations) | | | |
| Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable? | | X | |
| Does USP have labeling recommendations? If any, does ANDA meet them? | | X | |
| Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? | | X | |
| Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. | | | |
| Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) | | | |
| Insert labeling references a food effect or a no-effect? If so, was a food study done? | | X | |
| Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why. | | X | |
| Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. | | | |

NOTES/QUESTIONS TO THE CHEMIST: N. Fallon / 1/31/01

✓ 1. The labeling states that there is 30% alcohol (v/v) in this product. Is this accurate? Yes

✓ 2. Please verify that 6 sprays deliver 1 mL of solution. 0.1c (P416) Procedure verified

✓ 3. Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At the time the rule was passed, such closures were not yet available. However, firms must comply once they do become available. Clay-Park has committed to do so. This product is packaged in child resistant packaging.

FOR THE RECORD:

1. Labeling review based on the labeling for Rogaine Extra Strength for Men, 5% (NDA 20-834) – Pharmacia and Upjohn Consumer Healthcare; approved November 14, 1997.

2. Packaging
Rogaine packages its extra strength product in 1 x 60 mL and 2 x 60 mL cartons.

Clay-Park is proposing to package its white, HDPE 60 mL bottles in cartons of one. The primary closure and the dropper are child resistant. The sprayer is not.

Please note that a final rule was issued in November 1998 titled "Requirements for Child-Resistant Packaging; Minoxidil Preparations with More than 14 mg of Minoxidil per Package." According to this rule, all applicators accompanying this product that can replace the original closure of the packaging must also be child-resistant. At present, the sprayer is not child-resistant (see 16 CFR 1700.14(a)(28). At the time this rule was passed, child resistant closures for the sprayers were not yet available. However, firms must advise the Agency of their plans and comply once such closures do become available.

3. Labeling
Although the innovator calls its product "Rogaine Extra Strength for Men", the applicant has been asked to revise its labeling to use just the established name.

4. Inactive Ingredients
There do not appear to be discrepancies between the labeling and the C&C Statements.

5. USP Issues
USP – Preserve in tight containers
RLD – Store at CRT, 20-25°C (68-77°F).
ANDA – Store at CRT, 20-25°C (68-77°F). Clay-Park has been asked to include "Keep tightly closed" with its storage recommendation.

6. Bio Issues – Waiver granted 1/21/00.

7. Patents/Exclusivities – None pending.

---

Date of Review:

January 30, 2001

Date of Submission:

January 23, 2001 (Amendment)

Primary Reviewer:

LO Golson

Date:

1/30/01

Team Leader:

John D Grace

Date:

1/30/2001

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cc:

ANDA: 75-737
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
V:\FIRMSAM\CLAYPARK\LTRS&REV\75737ap.l
Review

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# CHEMISTRY REVIEWS

# OFFICE OF GENERIC DRUGS

## ABBREVIATED NEW DRUG APPLICATION
## CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. **CHEMIST□S REVIEW NO.#** 1 (one)

2. **ANDA #** 75-737

3. **NAME AND ADDRESS OF APPLICANT:**
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. **LEGAL BASIS OF SUBMISSION:**
The basis of Clay-Park's proposed ANDA for Minoxidil Topical Solution USP, 5%, is the reference listed drug, Rogaine® Extra Strength for Men, 5% (NDA 020-834) manufactured by Pharmacia & Upjohn. According to information published in the list of Approved Drug Products with Therapeutic Equivalence Evaluations, current through July 1999, Rogaine® Extra Strength for Men, 5% is entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act until November 14, 2000. Clay-Park Labs, Inc. does not intend to market this product prior to the expiration of this exclusivity marketing period.

The firm has certified that in its opinion and to the best of its knowledge, there are no patents that claim the listed drug referred in this application (page 0013).

Debarment Certification: Included (v1.4, page 1063)

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Minoxidil Topical Solution USP, 5%

8. **SUPPLEMENT(S) PROVIDE(S) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES:**
Applicant:
11-18-1999 Date of application
FDA:
01-04-2000 ANDA Acceptance letter

10. **PHARMACOLOGICAL CATEGORY:** Antialopecia agent, Antihypertensive

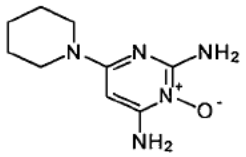
11. **Rx or OTC:** Over-The-Counter (OTC)

12. **RELATED IND/NDA/DMF(s):**
DMF [redacted] (b)(4) and [redacted] (b)(4) See section #37 for additional information.

13. **DOSAGE FORM:** Solution (Topical)

14. **STRENGTH:** 5%

15. **CHEMICAL NAME, STRUCTURE AND PHYSICAL PROPERTIES:**
Minoxidil. 2,4-Pyrimidinediamine, 6-(1- piperidinyl)-,3-oxide.
C9H15N5O - 209.25. 38304-91-5. Antihypertensive. USP 24, page 1118.



16. **COMMENTS:**
The following sections are *NOT SATISFACTORY:*
20. Component and Composition
23. Raw materials
25. Other firms
26. Manufacturing and processing
29. Laboratory controls
30. Stability
The following section is *PENDING*
32. Labeling

17. **CONCLUSIONS AND RECOMMENDATIONS:** Not approvable (Major - NA)

18. **RECORDS AND REPORTS:** N/A

19. **REVIEWER:** Neeru B. Takiar **DATE COMPLETED:** 04/18/00
Endorsed by D. Gill, Ph.D. Revised: 05/18/00

Following this page, 18 pages withheld in full (b)(4)

**38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT**

**NDA:** 75-737 **APPLICANT:** Clay-Park Labs, Inc.

**DRUG PRODUCT:** Minoxidil Topical Solution USP, 5%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4.

5.

6.

7.

8. (b) (4)

9.

10.

11.

12.

13.

14.

15.

16.

(b) (4)

17. [redacted]

18. [redacted]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please update your specifications for all excipients and provide the revised certificate of analysis to refer to USP 24.

2. The firms referenced in your ANDA relative to the manufacturing and testing of the product must be in compliance with CGMP at the time of approval.

3. You are advised that the use of in-house analytical methods for testing the drug product do not relieve you from meeting the compendial standards. In the event of a dispute, the USP method will be used in analyzing the drug product.

4. Your response must also address the labeling deficiencies.

Sincerely yours,

5/28/00

S/ Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-737
Field Copy
Division File

Endorsements:

HFD-623/N.Takiar/04-18-00; Revised 05-18-00 N. Takiar 5/18/00
HFD-623/D.Gill, Ph.D./ DGill 5-18-00
HFD-617/R.Yu/ RYu 5-18-00
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# OFFICE OF GENERIC DRUGS

## ABBREVIATED NEW DRUG APPLICATION
## CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. **CHEMISTRY REVIEW NO.# 2**

2. **ANDA #** 75-737

3. **NAME AND ADDRESS OF APPLICANT:**
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. **LEGAL BASIS OF SUBMISSION:**
The basis of Clay-Park's proposed ANDA for Minoxidil Topical Solution USP, 5%, is the reference listed drug, Rogaine® Extra Strength for Men, 5% (NDA 020-834) manufactured by Pharmacia & Upjohn. According to information published in the list of Approved Drug Products with Therapeutic Equivalence Evaluations, current through July 1999, Rogaine® Extra Strength for Men, 5% is entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act until November 14, 2000. Clay-Park Labs, Inc. does not intend to market this product prior to the expiration of this exclusivity marketing period.

The firm has certified that in its opinion and to the best of its knowledge, there are no patents that claim the listed drug referred in this application (page 0013).

Debarment Certification: Included (v1.4, page 1063)

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Minoxidil Topical Solution USP, 5%

8. **SUPPLEMENT(S) PROVIDE(S) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES:**
11-18-1999 Date of application
08-02-2000 Amendment-Response to deficiency letter dated 5/24/00

10. **PHARMACOLOGICAL CATEGORY:** Antialopecia agent, Antihypertensive

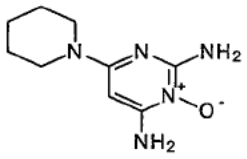
11. **Rx or OTC:** Over-The-Counter (OTC)

12. **RELATED IND/NDA/DMF(s):**
DMF [redacted] (b) (4) and [redacted] (b) (4) See section #37 for additional information.

13. **DOSAGE FORM:** Solution (Topical)

14. **STRENGTH:** 5%

15. **CHEMICAL NAME, STRUCTURE AND PHYSICAL PROPERTIES:**
Minoxidil. 2,4-Pyrimidinediamine, 6-(1- piperidinyl)-,3-oxide.
C9H15N5O - 209.25. 38304-91-5. Antihypertensive. USP 24, page 1118.



16. **COMMENTS:**
The following sections are *NOT SATISFACTORY:*
23. Drug Substance
26. Manufacturing and Processing
30. Stability
The following section is *PENDING*
32. Labeling

17. **CONCLUSIONS AND RECOMMENDATIONS:** Not Approvable (NA-FACSIMILE)

18. **RECORDS AND REPORTS:** N/A

19. **REVIEWER:** Neeru B. Takiar **DATE COMPLETED:** 12/12/00
Endorsed by D. Gill, Ph.D.

Following this page, 17 pages withheld in full (b)(4)

**38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT**

**ANDA:** 75-737 **APPLICANT:** Clay-Park Labs, Inc.

**DRUG PRODUCT:** Minoxidil Topical Solution USP, 5%

The deficiencies presented below represent FACSIMILE deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

Please submit data for review.

Sincerely yours,

DSGiles

for Rashmikant M. Patel, Ph.D. 12-25-00
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-737
Field Copy
Division File

Endorsements:

HFD-623/N.Takiar/12-12-00; Revised on 12-19-00 N. Takiar 12/22/00
HFD-623/D.Gill, Ph.D./12/19/00 12/22/00 for
HFD-617/R.Yu/12/19/00 Ryu 12/22/00
\\CDS008\WP51F99\FIRMSAM\CLAYPARK\LTRS&REV\75737.RV2.DOC
F/T by: DJ 12/20/00

NA-FACSIMILE

# OFFICE OF GENERIC DRUGS

## ABBREVIATED NEW DRUG APPLICATION
## CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. **CHEMISTRY REVIEW NO.# 3**

2. **ANDA #** 75-737

3. **NAME AND ADDRESS OF APPLICANT:**
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. **LEGAL BASIS OF SUBMISSION:**
The basis of Clay-Park's proposed ANDA for Minoxidil Topical Solution USP, 5%, is the reference listed drug, Rogaine® Extra Strength for Men, 5% (NDA 020-834) manufactured by Pharmacia & Upjohn. According to information published in the list of Approved Drug Products with Therapeutic Equivalence Evaluations, current through July 1999, Rogaine® Extra Strength for Men, 5% is entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act until November 14, 2000. Clay-Park Labs, Inc. does not intend to market this product prior to the expiration of this exclusivity marketing period.

The firm has certified that in its opinion and to the best of its knowledge, there are no patents that claim the listed drug referred in this application (page 0013).

Debarment Certification: Included (v1.4, page 1063)

5. **SUPPLEMENT(s):** N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Minoxidil Topical Solution USP, 5%

8. **SUPPLEMENT(S) PROVIDE(S) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**
11-18-1999 Date of application
01-23-2001 Fax amendment - Response to def. letter of 12/26/00

10. **PHARMACOLOGICAL CATEGORY:** Antialopecia agent, Antihypertensive

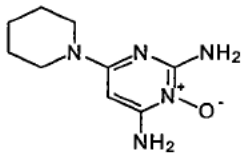
11. **Rx or OTC:** Over-The-Counter (OTC)

12. **RELATED IND/NDA/DMF(s):**
DMF [redacted] (b) (4) and [redacted] (b) (4) See section #37 for additional information.

13. **DOSAGE FORM:** Solution (Topical)

14. **STRENGTH:** 5%

15. **CHEMICAL NAME, STRUCTURE AND PHYSICAL PROPERTIES:**
Minoxidil. 2,4-Pyrimidinediamine, 6-(1- piperidinyl)-, 3-oxide. $C_9H_{15}N_5O$ 209.25. 38304-91-5. Antihypertensive. USP 24, page 1118.



16. **COMMENTS:** N/A

17. **CONCLUSIONS AND RECOMMENDATIONS:** Approvable
**pending acceptable EES**

18. **RECORDS AND REPORTS:** N/A

19. **REVIEWER:** Neeru B. Takiar **DATE COMPLETED:** 01/29/01
Endorsed by D. Gill, Ph.D.

Following this page, 7 pages withheld in full (b)(4)

cc: ANDA 75-737
Field Copy
Division File

Endorsements:

HFD-623/N.Takiar/01-29-01 N. Takiar 2/9/01
HFD-623/D.Gill, Ph.D./02-01-01 D. Sherbe 2/9/01
HFD-617/R.Yu/02-05-01 RY 2/9/01
\\CDS008\WP51F99\FIRMSAM\CLAYPARK\LTRS&REV\75737SOL.RV3.DOC
F/T by: 02-05-01

Approvable

# OFFICE OF GENERIC DRUGS

## ABBREVIATED NEW DRUG APPLICATION
## CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. **CHEMISTRY REVIEW NO.# 4**

2. **ANDA #** 75-737

3. **NAME AND ADDRESS OF APPLICANT:**
Clay-Park Labs, Inc
Attention: Candis Edwards
1700 Bathgate Ave
Bronx, NY 10457

4. **LEGAL BASIS OF SUBMISSION:**
The basis of Clay-Park's proposed ANDA for Minoxidil Topical Solution USP, 5%, is the reference listed drug, Rogaine® Extra Strength for Men, 5% (NDA 020-834) manufactured by Pharmacia & Upjohn. According to information published in the list of Approved Drug Products with Therapeutic Equivalence Evaluations, current through July 1999, Rogaine® Extra Strength for Men, 5% is entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act until November 14, 2000. Clay-Park Labs, Inc. does not intend to market this product prior to the expiration of this exclusivity marketing period.

The firm has certified that in its opinion and to the best of its knowledge, there are no patents that claim the listed drug referred in this application (page 0013).

Debarment Certification: Included (v1.4, page 1063)

5. **SUPPLEMENT(s)**: N/A

6. **PROPRIETARY NAME:** N/A

7. **NONPROPRIETARY NAME:** Minoxidil Topical Solution USP, 5%

8. **SUPPLEMENT(S) PROVIDE(S) FOR**: N/A

9. **AMENDMENTS AND OTHER DATES:**

| | |
|---|---|
| 11-18-1999 | Date of application |
| 03-05-2001 | New Correspondance - Informational Amendment |
| 09-06-2001 | Informational Amendment - Retest policy for Inactive Ingredients |
| 12-06-2001 | Minor Amendment - Response to deficiency |

letter dated
February 12, 2001

10. **PHARMACOLOGICAL CATEGORY:** Antialopecia agent, Antihypertensive

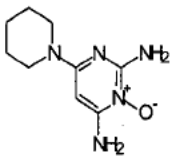
11. **Rx or OTC:** Over-The-Counter (OTC)

12. **RELATED IND/NDA/DMF(s):**
DMF [redacted] (b) (4) and [redacted] (b) (4). See section #37 for additional information.

13. **DOSAGE FORM:** Solution (Topical)

14. **STRENGTH:** 5%

15. **CHEMICAL NAME, STRUCTURE AND PHYSICAL PROPERTIES:**
Minoxidil. 2,4-Pyrimidinediamine, 6-(1- piperidinyl)-, 3-oxide.
$C_9H_{15}N_5O$ 209.25. 38304-91-5. Antihypertensive. USP 24, page 1118.



16. **COMMENTS:** N/A

17. **CONCLUSIONS AND RECOMMENDATIONS:** Approvable

18. **RECORDS AND REPORTS:** N/A

19. **REVIEWER:** Neeru B. Takiar **DATE COMPLETED:** 02/22/02
Endorsed by D. Gill, Ph.D.

Following this page, 7 pages withheld in full (b)(4)

cc: ANDA 75-737
Field Copy
Division File

Endorsements:

HFD-623/N.Takiar/02-22-02/2/28/02 N.Takiar 3/6/02
HFD-623/D.Gill, Ph.D./3/5/02 DSGill 3-7-02
HFD-617/R.Wu/3/5/02 RWu 3/7/02

V:\FIRMSAM\CLAYPARK\LTRS&REV\75737SOL.RV4.doc
F/T by: DJ 3/5/02

Approvable

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# BIOEQUIVALENCE REVIEWS

Minoxidil Topical Solution, USP
5 %
ANDA #75-737
Reviewer: James Chaney
V:\FIRMSAM\CLAYPARK\LTRS&REV\75737W.N99

Clay-Park Labs, Inc.
Bronx, New York
Submission Date:
November 18, 1999

**REVIEW OF A WAIVER REQUEST**

## I. Background

1. The firm has requested a waiver of *in vivo* bioequivalence study requirement for its proposed product, Minoxidil Topical Solution, 5%. The reference listed product is Rogaine® Extra Strength for Men, 5% Minoxidil Topical Solution, manufactured by Pharmacia and Upjohn.
2. Minoxidil Topical Solution is an OTC drug product indicated for hair regrowth treatment on the upper scalps of men.
3. The test and the reference listed product are both topical solutions.

## II. Formulation Comparison

The test and reference formulations are compared in the following table:

| Ingredient | Minoxidil Topical Solution, USP, 5% | Rogaine® Extra Strength Minoxidil 5% Topical Solution |
|---|---|---|
| | Percent Composition | Percent Composition |
| Minoxidil, USP | 5 % w/v | 5 % w/v |
| Propylene Glycol, USP | 50 % v/v | 50 % v/v |
| (b) (4) Alcohol (b) (4) USP | 30 % v/v | 30 % v/v |
| Purified Water, USP | Q.S. | Q.S. |

## III. Comments

1. The test product, Minoxidil Topical Solution, 5%, contains the same active ingredient in the same concentration and dosage form as the reference product, Rogaine® Extra Strength for Men, 5% Minoxidil Topical Solution. The test formulation does not contain any inactive ingredients known to significantly affect absorption of the active ingredient or drug moieties.

2. A waiver is granted under 21 CFR 320.22(b)(3), in that that the drug product is (i) a solution for application to the skin, (ii) contains an active drug ingredient or therapeutic moiety in the same dosage form as a drug product that is the subject of an approved full NDA, and (iii) contains no inactive ingredient or other change in formulation from the drug product that is the subject of the approved full new drug application that may significantly affect absorption of the active drug ingredient or active moiety.

## IV. Recommendation

The Division of Bioequivalence agrees that the information submitted by Clay-Park Labs, on its drug product, Minoxidil Topical Solution, 5%, falls under 21 CFR section 320.22 (b) (3) of the Bioavailability/ Bioequivalence Regulations. The waiver of an *in vivo* bioequivalence study on the drug product is granted. The Division of Bioequivalence deems the test product, Minoxidil Topical Solution, 5%, bioequivalent to the reference product, Rogaine® Extra Strength for Men, 5% Minoxidil Topical Solution, manufactured by Pharmacia and Upjohn.

James E. Chaney

James E. Chaney, Ph.D.
Division of Bioequivalence
Review Branch I

RD INITIALED YCHuang
FT INITIALED YCHuang

Date 1/19/00

Concur: Dale P. Conner

Date 1/21/00

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

JEC/011800
V:\FIRMSAM\CLAYPARK\LTRS&REV\75737W.N99

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-737 APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Minoxidil Topical Solution, 5%

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# ANDA 075737

# ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ANDA 75-737

Clay-Park Labs, Inc.
Attention: Candis Edwards
1700 Bathgate Ave.
Bronx, NY 10457

JAN 4 2000

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Minoxidil Topical Solution USP, 5%

DATE OF APPLICATION: November 18, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 19, 1999

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Joe Buccine
Project Manager
(301) 827-5848

Sincerely yours,

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-737
cc: DUP/Jacket
Division File
Field Copy
HFD-610/R.West
HFD-610/P.Rickman
HFD-92
HFD-615/M.Bennett
Endorsement:
HFD-615/ NMahmud, Chief, RSB _____ date 1/3/00
HFD-615, PPatel, CSO Pmar Patel _____ date 12/13/99
HFD-600, PSchwartz, Sup. Chem. _____ date
Word File V:\Filesam\Clay-Park\ltrs&rev\75737.ack
F/T mjl/12/13/99
ANDA Acknowledgment Letter!

# MAJOR AMENDMENT

MAY 24 2000

ANDA 75-737

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Clay-Park Labs, Inc. PHONE: 718-960-9976

ATTN: Candis Edwards FAX: 718-960-0111

FROM: Ruby Yu PROJECT MANAGER (301) 827–5848

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated November 18, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Minoxidil Topical Solution USP, 5%.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments ( 6 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

## SPECIAL INSTRUCTIONS:

Chemistry, Labeling, and Bioequivalency comments are provided.



X:\new\ogdadmin\macros\faxmaj.frm

Ryu 5-24-00

MAY 24 2000

**38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT**

**ANDA:** 75-737 **APPLICANT:** Clay-Park Labs, Inc.

**DRUG PRODUCT:** Minoxidil Topical Solution USP, 5%

The deficiencies present (b) (4) below represent MAJOR deficiencies.

A. Deficiencies:

1. (b) (4)
2.
3.
4.
5.
6.
7.

8. [redacted] (b) (4)

9.

10.

11.

12.

13.

14.

15.

16.

17. (b) (4)

18.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. Please update your specifications for all excipients and provide the revised certificate of analysis to refer to USP 24.

2. The firms referenced in your ANDA relative to the manufacturing and testing of the product must be in compliance with CGMP at the time of approval.

3. You are advised that the use of in-house analytical methods for testing the drug product do not relieve you from meeting the compendial standards. In the event of a dispute, the USP method will be used in analyzing the drug product.

4. Your response must also address the labeling deficiencies.

Sincerely yours,

S/ Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

# RECORD OF TELEPHONE CONVERSATION

Reference is made to the deficiency letter issued by OGD on May 24, 2000 and the firm's fax dated June 7, 2000.

Deficiency #4
OGD acknowledged the firm's comments regarding [redacted] (b) (4)
The firm's comment about [redacted] (b) (4) is acceptable.

Deficiency #6
Regarding [redacted] (b) (4) will be acceptable.

Deficiency #7
The firm must distinguish between [redacted] (b) (4)

Deficiency #9
Although testing of [redacted] (b) (4) (b) (4) (b) (4) from the ANDA and commit to resolve the issue with the district office.

Deficiency #12
OGD acknowledged the location of the Master Packaging Record.

Deficiency #13
a. The firm will provide information on the [redacted] (b) (4)

d. The firm stated they never [redacted] (b) (4) ".

Deficiency #14
Regarding [redacted] (b) (4), OGD acknowledged the firm's comment.

Deficiency #15
The firm stated the product [redacted] (b) (4) will do testing for informational purposes and for added assurance of the quality of the product. The firm will provide an explanation in their response.

Deficiency #16
The firm stated they only have data on [redacted] (b) (4) and will provide all available data up to the time of approval.

Deficiency # 18
Refer to #13

**DATE:**
June 9, 2000

**ANDA NUMBER:**
75-737

**PRODUCT NAME:**
Minoxidil Topical Solution USP, 5%

**FIRM NAME:**
Clay-Park Labs, Inc.

**FIRM REPRESENTATIVE:**
Candis Edwards
[redacted] (b) (6)

**PHONE NUMBER:**
718-960-9976

**FDA REPRESENTATIVES:**
Dave Gill
Neeru Takiar
Ruby Yu

**SIGNATURES:**

Dave Gill DSG 6/16/00
Neeru Takiar NT 6/16/00
Ruby Yu RY 6/16/00

CC: ANDA 75-737
Telecon Binder

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# FAX AMENDMENT

DEC 26 2000

ANDA 75-737

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Clay-Park Labs

TEL: 718-960-9976

ATTN: Candis Edwards

FAX: 718-960-0111 (olc per Ms Mis La)

FROM: Ruby Yu

PROJECT MANAGER: 301-827-5848

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated November 18, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Minoxidil Topical Solution USP, 5%.

Reference is also made to your amendment(s) dated: August 2, 2000.

Attached are 1 pages of minor deficiencies and/or comments that should be responded to within 30 calendar days from the date of this document. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your complete response should be (1) faxed directly to our document control room at 301- 827-4337, (2) mailed directly to the above address, and (3) the cover sheet should be clearly marked a FAX AMENDMENT.

Please note that if you are unable to provide a complete response within 30 calendar days, the file on this application will be closed as a MINOR AMENDMENT and you will be required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Accordingly, a response of greater than 30 days should be clearly marked MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Facsimiles or incomplete responses received after 30 calendar days will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. Further if a major deficiency is cited in the bioequivalence review, the subsequent Not Approvable letter will request that the reply be declared a MAJOR AMENDMENT.

**SPECIAL INSTRUCTIONS:**

Chemistry comments provided. Labeling comments, if any, will be provided when the review is completed.



RYu 12-26-00

DEC 26 2007

**38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT**

**ANDA:** 75-737 **APPLICANT:** Clay-Park Labs, Inc.

**DRUG PRODUCT:** Minoxidil Topical Solution USP, 5%

The deficiencies presented below represent FACSIMILE deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

Sincerely yours,

DSGiii

for Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

# RECORD OF TELEPHONE CONVERSATION

Reference is made to the deficiency letter issued by OGD on December 26, 2000 and the firm's fax dated January 2, 2001 requesting clarification on deficiencies #1 and #2.

#1 (b) (4)
The firm agreed to (b) (4)
(b) (4)

#2 (b) (4)
The firm will address the following issues:

- (b) (4)

A follow-up t-con was placed to Candis Edwards in reference to deficiency #2. The firm will provide explanation of the (b) (4)

**DATE:**
January 3, 2001

**ANDA NUMBER:**
75-737

**PRODUCT NAME:**
Minoxidil Topical Solution USP, 5%

**FIRM NAME:**
Clay-Park Labs, Inc.

**FIRM REPRESENTATIVE:**
Candis Edwards
(b) (6)

**PHONE NUMBER:**
718-960-9976

**FDA REPRESENTATIVES:**
Dave Gill
Neeru Takiar
Ruby Yu

**SIGNATURES:**

Dave Gill
Neeru Takiar NT 1/12/01
Ruby Yu DSG for 1-12-01
1-12-00

CC: ANDA 75-737
Telecon Binder

V:\FIRMSAM\CLAYPARK\TELECONS\75737.TC.010301.DOC

# ANDA APPROVAL SUMMARY

| ANDA: | CHEMIST: | DATE: |
|---|---|---|
| 75-737 | Neeru Takiar | January 29, 2001 |

**DRUG PRODUCT:**
Minoxidil Topical Solution USP, 5%

**FIRM:**
Clay-Park Labs, Inc.

| DOSAGE FORM: | STRENGTH: |
|---|---|
| Solution | 5% |

**cGMP:**
EER **Withhold** on January 22, 2001; new site added 2/1/2001, pending overall recommendation.

**BIO:**
Acceptable on January 19, 2000; Signed off on January 21, 2000.

**VALIDATION *(Description of dosage form same as firm's):***
The DS and DP are covered by the monographs under USP 24. No validation is required.

**STABILITY:**
The containers in the stability studies are identical to those in the container section.

**LABELING:**
Acceptable January 30, 2001

**STERILIZATION VALIDATION *(If applicable)*:**
Not applicable.

**SIZE OF BIO BATCH *(Firm's source of NDS ok?)*:**
The bio batch (RX017) size is (b) (4)

**SIZE OF STABILITY BATCHES *(If different from bio batch, were they Manufactured via the same process?)*:**
Same as the bio batch.

**PROPOSED PRODUCTION BATCH MANUFACTURING PROCESS THE SAME?**
The size of proposed production batches is (b) (4). The manufacturing processes are identical, (b) (4)

| Signature of chemist: | Signature of supervisor: |
|---|---|
| Neeru B. Takiar 1/29/01 N. Takiar 2/9/01 | Dave Gill, Ph.D. 1/30/01 Stephen Hill 2/9/01 |

V:\FIRMSAM\CLAYPARK\LTRS&REV\75737APSUM.DOC

ANDA 75-737

Clay-Park Labs, Inc.
Attention: Candis Edwards
1700 Bathgate Ave.
Bronx, NY 10457

FEB 12 2001

Dear Madam:

This is in reference to your abbreviated new drug application dated November 18, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Minoxidil Topical Solution USP, 5% (For Men).

Reference is also made to your amendment dated January 23, 2001.

We have completed the review of this abbreviated application and have concluded that this application is deficient and, therefore, not approvable under 21 CFR 314.125 (b)(13) because the Center for Drug Evaluation and Research (CDER) is unable to find that the methods used in, and the facilities and controls used for, the manufacture, processing, packaging or holding of the drug product, Minoxidil Topical Solution USP, by Clay-Park Labs., Inc. in Bronx, NY comply with current good manufacturing practice (cGMP) regulations.

Our conclusion is based upon a recommendation we received from our Division of Manufacturing and Product Quality (DMPQ), Office of Compliance, to withhold approval of your abbreviated application.

Until such time that you can demonstrate to the Agency that the problems have been corrected and the Agency's concerns are otherwise satisfied, your application cannot be approved.

In addition, the control testing facility, [redacted] (b) (4) that is utilized to conduct testing of the active drug substance, minoxidil, USP, is out of business as of [redacted] (b) (4). Please provide a new testing facility to perform the tests.

You should amend this application when the CGMP-related issues have been satisfactorily resolved. Your amendment to the application submitted in response to this not approvable letter will be considered a MINOR AMENDMENT provided that the amendment contains no significant additional information necessary to remedy the cGMP problems. Please include a statement from a responsible corporate official certifying that your facilities

have been found to be in compliance with cGMPs and have been cleared for approval of the drug product by representatives of the local FDA District Office. If, as a result of follow-up inspections related to the ongoing evaluation of this or other applications, it is necessary for you to significantly revise your procedures, controls or practices to correct the deficiencies, then the amendment will be considered to represent a MAJOR AMENDMENT. Your amendment should be plainly marked as such in your cover letter.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120, which will either amend or withdraw this application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

R R Patel 2/9/01

Rashmikant M. Patel, Ph.D
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-737
Division File
Field Copy

Endorsements:
HFD-623/N.Takiar/ N-Takiar 2/9/01
HFD-623/D.Gill/ D. Gill 2/9/01
HFD-617/R.Yu./2/7/01 R Yu 2/9/01

F/T by: DJ 2/7/01

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MINOR DEFICIENCY

BC & Team
Thelma Brooks
2/12/01

# OGD APPROVAL ROUTING SUMMARY

ANDA # 75-737 Applicant Clay-Park Labs, INC.
Drug Minoxidil Topical Solution USP Strength 5 %

* OTC *
APPROVAL ☒ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

| REVIEWER: | DRAFT RECEIPT | FINAL ACTION |
|---|---|---|
| 1. Project Manager Ruby Yu IV | Date 2/1/01 | Date 2/9/01 |
| Review Support Br | Initials RYu | Initials RYu |

**Application Summary:**

Original Rec'd date 11/19/1999
Date Acceptable for Filing 11/19/1999
Patent Certification (type) II
Date Patent/Exclus.expires 11/14/2000
Citizens Petition/Legal Case Yes ☐ No ☒
(If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒
(If YES, check PETS)
Pediatric Exclusivity Tracking System(PETS)
Date checked _____ NDA# _____
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

EER Status Pending ☐ Acceptable ☐ OAI ☒
Date of EER Status Withhold 2/6/01
Date of Office Bio Review 1/21/2000
Date of Labeling Approv. Sum 1/30/2001
Date of Sterility Assur. App. N/A
Methods Val. Samples Pending Yes ☐ No ☒
30 Day Clock Start _____ End _____
Commitment Rcd. from Firm Yes ☐ No
Modified-release dosage form: Yes ☐ No ☒

Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def./N/A Minor issued ☐ Date _____
Comments:

| | | |
|---|---|---|
| 2. Div. Dir./~~Deputy Dir.~~ | Date 2/9/01 | Date 2/9/01 |
| Chemistry Div. I ~~or II~~ | Initials RRC | Initials RFS |

Comments:
NA letter issued / DI tested [redacted] (b) (4) ic ont of business/WITHHELD for CGMP

| | | |
|---|---|---|
| 3. Frank Holcombe | Date _____ | Date _____ |
| Assoc. Dir. For Chemistry | Initials _____ | Initials _____ |

Comments: (First generic drug review)

| | | |
|---|---|---|
| 4. Pat Beers Block | Date 2/12/01 | Date 2/12/01 |
| Supv. Review Support Branch | Initials PBB | Initials PBB |

EER Status: ~~Unacceptable~~ - See

Bioequivalence sites:
Clinical site: N/A waiver granted
Inspection needed: ☐ yes ☐ no
Status: ☐acceptable ☐unacceptable ☐ pending
Date of status: _____
Reason:

Analytical site: N/A waiver granted
Inspection needed: ☐ yes ☐ no
Status: ☐acceptable ☐unacceptable ☐pending
Date of status: _____
Reason:

Bioequivalence office level sign off:
Waiver granted 1/21/00. Bio sign off completed 1/21/00.
Labeling Status: Acceptable 1/30/2001

Microbiology status: N/A

Patent Certification: Para II; no exclusivity granted & RLD Expired 11/14/2000
Controlled Correspondence/Cit.Pet: N/A
Comments: RLD = 20-834

Minor Def letter to issue.
PBB

**REVIEWER:** **DRAFT RECEIPT** **FINAL ACTION**

5. Nasser Mahmud — Date_____ Date_____
Supv. Reg. Support Branch — Initials_____ Initials_____

Contains GDEA certification: Yes ☐ No ☐ Determ. of Involvement? Yes ☐ No ☐
(required if sub after 6/1/92) Pediatric Exclusivity System
Patent/Exclusivity Certification: Yes ☐ No ☐ Date Checked _____
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐
Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☐
Comments:

6. Peter Rickman — Date_____ Date_____
Acting Director, DLPS — Initials_____ Initials_____
Comments:

7. Robert L. West — Date _____ Date _____
Acting Deputy Director, OGD — Initials_____ Initials _____

Para.IV Patent Cert: Yes☐ No☐; Pending Legal Action:Yes☐ No☐; Petition:Yes☐ No☐
Comments:

8. Gary Buehler — Date _____ Date _____
Acting Director, OGD — Initials _____ Initials _____
Comments:

First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐

9. Project Manager — Date_____ Date_____
Review Support Branch — Initials_____ Initials _____

_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
_____Time notified of approval by phone _____Time approval letter faxed

FDA Notification:
_____Date e-mail message sent to "OGD approvals" account
_____Date Approval letter copied to"//cder/drugapp" directory

v:\reports\approval\approvrou

OGD APPROVAL ROUTING SUMMARY

ANDA # 75-737 Applicant Clay Park Labs
Drug Minoxidil Topical Solution USP Strength 5%

OVAL X OTC TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

REVIEWER: | DRAFT RECEIPT | FINAL ACTION

1. Project Manager Ruby Wu IV — Date 3/5/02 — Date 3/7/02
Review Support Br — Initials RWu — Initials RWu

Application Summary:
Original Rec'd date 11/19/1999
Date Acceptable for Filing 11/19/1999
Patent Certification (type) II
Date Patent/Exclus. expires 11/14/00
Citizens Petition/Legal Case Yes ☐ No X
(If YES, attach email from PM to CP coord)
First Generic Yes ☐ No X
(If YES, check PETS)
Pediatric Exclusivity Tracking PETS)
Date checked _____ NDA# _____
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

EER Status Pending ☐ Acceptable X OAI ☐
Date of EER Status 1/25/02
Date of Office Bio Review 1/21/00
Date of Labeling Approv. Sum 1/30/01
Date of Sterility Assur. App. N/A
Methods Val. Samples Pending Yes ☐ No X
30 Day Clock Start _____ End _____
Commitment Rcd. from Firm Yes ☐ No ☐
Modified-release dosage form: Yes ☐ No X
Interim Dissol. Specs in AP Ltr: Yes ☐

Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def./N/A Minor issued X Date 2/12/01
Comments:

2. Div. Dir./~~Deputy Dir.~~ — Date 3/8/02 — Date 3/8/02
Chemistry Div. I ~~or II~~ — Initials RR — Initials RR
Comments:

The Correction is satisfactory.

3. Frank Holcombe — Date _____ — Date _____
Assoc. Dir. For Chemistry — Initials _____ — Initials _____
Comments: (First generic drug review)

N/A Multiple generic approvals

4. Pat Beers Block — Date _____ — Date _____
Supv., Review Support Branch — Initials _____ — Initials _____
EER Status:

Refer to DLPS review below

Bioequivalence sites:
Clinical site:
Inspection needed: ☐ yes ☐ no
Status: ☐acceptable ☐unacceptable ☐ pending
Date of status: _____
Reason:

Analytical site:
Inspection needed: ☐ yes ☐ no
Status: ☐acceptable ☐unacceptable ☐pending
Date of status: _____
Reason:

Bioequivalence office level sign off: 3/15/02

Labeling Status:

Microbiology status:
Patent Certification:
Controlled Correspondence/Cit.Pet:
Comments: RLD =

/IEWER: | DRAFT RECEIPT | FINAL ACTION

Greg Davis
Supv., Reg. Support Branch
Date 3/15/02 Initials RW | Date 3/15/02 Initials RW for

Contains GDEA certification: Yes X No ☐ (required if sub after 6/1/92)
Determ. of Involvement? Yes ☐ No X
Pediatric Exclusivity System
Patent/Exclusivity Certification: Yes X No ☐
If Para. IV Certification- did applicant
Date Checked N/A
Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐
Written request issued ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐
Study Submitted ☐
Has case been settled: Yes ☐ No ☐
Date settled:
Is applicant eligible for 180 day
Generic Drug Exclusivity for each strength: Yes ☐ No X
Comments: There are no unexpired patents or exclusivity on the RLD.

RLD = Rogaine Extra Strength 5% (for Men) Pharmacia and Upjohn Co. NDA 20-834

Peter Rickman
Acting Director, DLPS
Date 3/15/02 Initials RW | Date 3/15/02 Initials RW for
Comments: Acceptable EES dated 1/25/02 (Verified 3/15/02). No OAI alerts noted. Bioequivalence waiver granted 1/19/00 under 21 CFR 320.22(b)(3). Office level bioendorsed 1/21/00. FRL acceptable 1/20/00 (as endorsed 1/02). CMC acceptable 3/7/02. Methods validation is not required - both the API and the drug product are in the USP (compendial).

Robert L. West
Acting Deputy Director, OGD
Date 3/15/02 Initials RW | Date 3/15/2002 Initials Robert West

Para. IV Patent Cert: Yes☐ No☐; Pending Legal Action: Yes☐ No☐; Petition: Yes☐ No☐
Comments: With the exception of CSR's, this application was acceptable from a review standpoint in Feb. 2001. Clay Park now has an acceptable recommendation from O.C.
THIS ANDA IS RECOMMENDED FOR APPROVAL.

8. Gary Buehler
Director, OGD
Comments:
Date 3/15/02 Initials RW | Date 3/15/2002 Initials RW for

First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg. Issue ☐

9. Project Manager Ruby Wu
Review Support Branch
Date 3/15/02 Initials RW | Date 3/15/02 Initials RW

N/A Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
2:55PM 3/15 Time notified of approval by phone 3:00 3/18 Time approval letter faxed

FDA Notification:
3/15/02 Date e-mail message sent to "OGD approvals" account
3/15/02 Date Approval letter copied to "//cder/drugapp" directory

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