CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

75-774

Generic Name: Ammonium Lactate Cream, 12 % (base)

Sponsor: Clay-Park Labs, Inc.

Approval Date: May 1, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
75-774

CONTENTS

Reviews / Information Included in this ANDA Review.	
Approval Letter	X
Tentative Approval Letter	
ANDAs	
Approvable Letter	
Final Printed Labeling	X
Medical Review(s)	X
Chemistry Review(s)	X
EA/FONSI	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology & Biopharmaceutics Reviews	
Bioequivalence Review(s)	X
Administrative Document(s)	X
Correspondence	X

ANDA 75-774

MAY 1 2002

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

Dear Madam:

This is in reference to your abbreviated new drug application dated December 29,1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ammonium Lactate Cream, 12% (base).

Reference is also made to your amendments dated December 5, 2001 and April 17, 2002.

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 labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Ammonium Lactate Cream, 12% (base) to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Lac-Hydrin® Cream 12% (base) of Westwood-Squibb Pharmaceuticals Inc.).

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.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising,

and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/

Gary Buehler 5/1/02
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-774

Final Printed Labeling

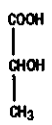
AMMONIUM LACTATE CREAM 12%*

FOR DERMATOLOGIC USE ONLY.
Not for ophthalmic, oral or intravaginal use.

Rx only

DESCRIPTION
*Ammonium lactate cream is a formulation of 12% lactic acid neutralized with ammonium hydroxide, as ammonium lactate, with a pH of 4.4 - 5.4. Ammonium lactate cream also contains water, light mineral oil, glyceryl stearate, PEG-100 stearate, propylene glycol, polyoxyl 40 stearate, glycerin, cetyl alcohol, magnesium aluminum silicate, polyoxyethylene 4 lauryl ether, methyl and propyl parabens, and methylcellulose.

Lactic acid is a racemic mixture of 2-hydroxypropanoic acid and has the following structural formula:



CLINICAL PHARMACOLOGY
Lactic acid is an alpha-hydroxy acid. It is a normal constituent of tissues and blood. The alpha-hydroxy acids (and their salts) are felt to act as humectants when applied to the skin. This property may influence hydration of the stratum corneum. In addition, lactic acid, when applied to the skin, may act to decrease corneocyte cohesion. The mechanism(s) by which this is accomplished is not yet known.

An *in vitro* study of percutaneous absorption of ammonium lactate cream using human cadaver skin indicates that approximately 6.1% of the material was absorbed after 68 hours.

INDICATIONS AND USAGE
Ammonium lactate cream is indicated for the treatment of ichthyosis vulgaris and xerosis.

CONTRAINDICATIONS
None known.

MAY -1 2002 APPROVED

WARNING
Use of this product should be discontinued if hypersensitivity to any of the ingredients is noted. Sun exposure to areas of the skin treated with ammonium lactate cream should be minimized or avoided (see PRECAUTIONS section).

PRECAUTIONS
General: For external use only. Stinging or burning may occur when applied to skin with fissures, erosions, or that is otherwise abraded (for example, after shaving the legs). Caution is advised when used on the face because of the potential for irritation. The potential for post-inflammatory hypo-or hyperpigmentation has not been studied.

Information for patients: Patients using ammonium lactate cream should receive the following information and instructions:

1. This medication is to be used as directed by the physician, and should not be used for any disorder other than for which it was prescribed. It is for external use only. Avoid contact with eyes, lips, or mucous membranes.

2. Patients should minimize or avoid use of this product on areas of the skin that may be exposed to natural or artificial sunlight, including the face. If sun exposure is unavoidable, clothing should be worn to protect the skin.

3. This medication may cause stinging or burning when applied to skin with fissures, erosions, or abrasions (for example, after shaving the legs).

4. If the skin condition worsens with treatment, the medication should be promptly discontinued.

Carcinogenesis, Mutagenesis, Impairment of Fertility: The topical treatment of CD-1 mice with 12%, 21% or 30% ammonium lactate formulations for two years did not produce a significant increase in dermal or systemic tumors in the absence of increased exposure to ultraviolet radiation. The maximum systemic exposure of the mice in this study was 0.7 times the maximum possible systemic exposure in humans. However, a long-term photocarcinogenicity study in hairless albino mice suggested that topically applied 12% ammonium lactate cream enhanced the rate of ultraviolet light-induced skin tumor formation.

The mutagenic potential of ammonium lactate cream was evaluated in the Ames assay and in the mouse *in vivo* micronucleus assay, both of which were negative.

In dermal Segment I and III studies with ammonium lactate cream there were no effects observed in fertility or pre- or post-natal development parameters in rats at dose levels of 300 mg/kg/day (1800 mg/m^2/day), approximately 0.4 times the human topical dose.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Animal reproduction studies have been performed in rats and rabbits at doses up to 0.7 and 1.5 times the human dose, respectively (600 mg/kg/day, corresponding to 3600 mg/m^2/day in the rat and 7200 mg/m^2/day in the rabbit) and have revealed no evidence of impaired fertility or harm to the fetus due to ammonium lactate cream. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, ammonium lactate cream should be used during pregnancy only if clearly needed.

Nursing Mothers: Although lactic acid is a normal constituent of blood and tissues, it is not known to what extent this drug affects normal lactic acid levels in human milk. Because many drugs are excreted in human milk, caution should be exercised when ammonium lactate cream is administered to a nursing woman.

Pediatric Use: Pediatric use information is approved for Bristol-Myers Squibb Company's ammonium lactate cream 12%. However, due to Bristol-Myers Squibb's marketing exclusivity rights, this drug product is not labeled for pediatric use.

ADVERSE REACTIONS
In controlled clinical trials of patients with ichthyosis vulgaris, the most frequent adverse reactions in patients treated with ammonium lactate cream were rash (including erythema and irritation) and burning/stinging. Each was reported in approximately 10–15% of patients. In addition, itching was reported in approximately 5% of patients.

In controlled clinical trials of patients with xerosis, the most frequent adverse reactions in patients treated with ammonium lactate cream were transient burning, in about 3% of patients, stinging, dry skin and rash, each reported in approximately 2% of patients.

DOSAGE AND ADMINISTRATION
Apply to the affected areas and rub in thoroughly. Use twice daily or as directed by a physician.

HOW SUPPLIED
Ammonium lactate cream is available in cartons of 280 g (2-140 g plastic tubes).

Store at controlled room temperature, 15° to 30°C (59° to 86°F).

Mfg. By: Clay-Park Labs, Inc.
Bronx, NY 10457

I493-4X
0402

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-774

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 1 (one)

2. ANDA # 75-774

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

4. LEGAL BASIS FOR SUBMISSION
The listed drug is Lac-Hydrin® 12% (ammonium lactate)Cream , the subject of NDA # 020508, approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc. containing ammonium acetate equivalent to 12% lactic acid.
Lac-Hydrin® 12% (ammonium lactate cream) Cream is listed in the Electronic Orange Book, Approved Drug Products with Therapeutic Equivalence Evaluations, current through September 1999. There is no unexpired marketing exclusivity for Lac-Hydrin® 12% (ammonium lactate cream) Cream.
Patent certification: paragraph II certification
Clay-Park Labs Inc. certifies that the patent #4,105,783 (Yu et al.) issued August 8, 1978, has expired. (the expiration date of the patent was not later than January 15, 1997.)

5. SUPPLEMENT(s)
None

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Ammonium Lactate Cream 12%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
None

9. AMENDMENTS AND OTHER DATES:
Date of submission: December 29, 1999
Amendment: March 16, 2000 (Response to refusal to file letter)

10. PHARMACOLOGICAL CATEGORY
treatment of ichthyosis vulgaris and xerosis

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
NDA # 020508, Lac-Hydrin® 12% (ammonium lactate)Cream , approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc.

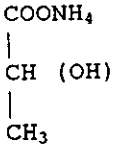
13. DOSAGE FORM
Cream

14. POTENCY
12%

15. CHEMICAL NAME AND STRUCTURE

DL-Lactic acid ammonium salt, $C_3H_9NO_3$, $CH_3CH(OH)COONH_4$

Chemical Structure:



16. RECORDS AND REPORTS

None

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

This application is not approvable.

19. REVIEWER: Liang-Lii Huang, Ph.D.
DATE COMPLETED: August 31, 2000
Endorsed by Paul Schwartz, Ph.D./August 31, 2000

APPEARS THIS WAY
ON ORIGINAL

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1. CHEMISTRY REVIEW NO. 2

2. ANDA # 75-774

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

4. LEGAL BASIS FOR SUBMISSION
The listed drug is Lac-Hydrin® 12% (ammonium lactate)Cream , the subject of NDA # 020508, approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc. containing ammonium acetate equivalent to 12% lactic acid.
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Patent certification: paragraph II certification
Clay-Park Labs Inc. certifies that the patent #4,105,783 (Yu et al.) issued August 8, 1978, has expired. (the expiration date of the patent was not later than January 15, 1997.)

5. SUPPLEMENT(s)
None

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Ammonium Lactate Cream 12%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
None

9. AMENDMENTS AND OTHER DATES:
Date of submission: December 29, 1999
Amendment: March 16, 2000 (Response to refusal to file letter)
~~Amendment 10/5/00~~ 9-20-00 nN
Amendment 10/5/00

10. PHARMACOLOGICAL CATEGORY
Treatment of ichthyosis vulgaris and xerosis

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
NDA # 020508, Lac-Hydrin® 12% (ammonium lactate)Cream , approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc.

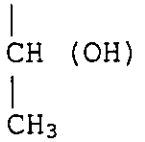
13. DOSAGE FORM
Cream

14. POTENCY
12%

15. CHEMICAL NAME AND STRUCTURE

DL-Lactic acid ammonium salt, $C_3H_9NO_3$, $CH_3CH(OH)COONH_4$

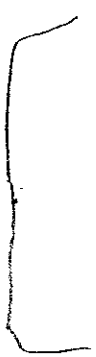
Chemical Structure:



16. RECORDS AND REPORTS

None

17. COMMENTS



18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 12/5/00

Supervisor: Paul Schwartz, Ph.D.

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information

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 75-774

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

4. LEGAL BASIS FOR SUBMISSION
The listed drug is Lac-Hydrin® 12% (ammonium lactate)Cream , the subject of NDA # 020508, approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc. containing ammonium acetate equivalent to 12% lactic acid.
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Patent certification: paragraph II certification
Clay-Park Labs Inc. certifies that the patent #4,105,783 (Yu et al.) issued August 8, 1978, has expired. (the expiration date of the patent was not later than January 15, 1997.)

5. SUPPLEMENT(s)
None

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Ammonium Lactate Cream 12%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
None

9. AMENDMENTS AND OTHER DATES:
Date of submission: December 29, 1999
Amendment: March 16, 2000 (Response to refusal to file letter)
Amendment 9/20/00
Amendment 10/5/00
Amendment 2/1/01
Amendment 6/28/01

10. PHARMACOLOGICAL CATEGORY
Treatment of ichthyosis vulgaris and xerosis

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
NDA # 020508, Lac-Hydrin® 12% (ammonium lactate)Cream , approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc.

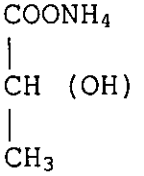
13. DOSAGE FORM
Cream

14. POTENCY
12%

15. CHEMICAL NAME AND STRUCTURE

DL-Lactic acid ammonium salt, $C_3H_9NO_3$, $CH_3CH(OH)COONH_4$

Chemical Structure:



16. RECORDS AND REPORTS

None

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable. (pending EER)

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 4/20/01

Supervisor: Paul Schwartz, Ph.D. 4/20/01

cc: ANDA 75-774
Division File
Field Copy

Endorsements:

HFD-627/NNashed/
HFD-627/PSchwartz
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F/t by: gp/7/27/01

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MINOR AMENDMENT

DEC 14 2000

ANDA 75-774

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.

TEL: (718) 960-9976

ATTN: Candis Edwards

FAX: (718) 960-0111

FROM: Elaine Hu

PROJECT MANAGER: 301-827-5848

Dear Madam :

This facsimile is in reference to your abbreviated new drug application dated December 29, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ammonium Lactate Cream, 12%.

Reference is also made to your amendment(s) dated: September 20 and October 5, 2000.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachment (_1_ page). 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 MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR 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 you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Bioequivalence and Labeling are still under review. Comments, if any, will be communicated to you under separate cover.

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1. CHEMISTRY REVIEW NO. 4

2. ANDA # 75-774

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

4. LEGAL BASIS FOR SUBMISSION
The listed drug is Lac-Hydrin® 12% (ammonium lactate) Cream , the subject of NDA # 020508, approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc. containing ammonium acetate equivalent to 12% lactic acid.
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Patent certification: paragraph II certification
Clay-Park Labs Inc. certifies that the patent #4,105,783 (Yu et al.) issued August 8, 1978, has expired. (the expiration date of the patent was not later than January 15, 1997.)

5. SUPPLEMENT(s)
None

6. PROPRIETARY NAME
None

7. NONPROPRIETARY NAME
Ammonium Lactate Cream 12%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
None

9. AMENDMENTS AND OTHER DATES:
Date of submission: December 29, 1999
Amendment: March 16, 2000 (Response to refusal to file letter)
Amendment 9/20/00
Amendment 10/5/00
Amendment 2/1/01
Amendment 6/28/01
Amendment 12/5/01 - Minor Amendment
Amendment 4/17/02 - Labeling Amendment

10. PHARMACOLOGICAL CATEGORY
Treatment of ichthyosis vulgaris and xerosis

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
NDA # 020508, Lac-Hydrin® 12% (ammonium lactate)Cream , approved August 29, 1996, held by Westwood-Squibb Pharmaceuticals Inc.

13. DOSAGE FORM

Cream

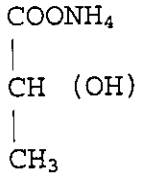
14. POTENCY

12%

15. CHEMICAL NAME AND STRUCTURE

DL-Lactic acid ammonium salt, $C_3H_9NO_3$, $CH_3CH(OH)COONH_4$

Chemical Structure:



16. RECORDS AND REPORTS

None

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER: DATE COMPLETED:

Nashed E. Nashed, Ph.D. 1/16/02

/S/ 4/30/02

Supervisor: James M. Fan 2/6/02

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-774

MEDICAL OFFICER REVIEW

MEDICAL OFFICER REVIEW
July 13, 2001

ANDA 75-774
Drug Product: Ammonium Lactate Cream, 12%
Sponsor: Clay-Park Labs, Inc.

The Division of Scientific Investigation has completed their inspection and submitted their report. They have identified several issues that need to be considered in the final decision. Patient #134 could potentially be considered a protocol violation/deviation. Exclusion of this patient from the evaluable population would not change the conclusion that this study is demonstrates bioequivalence of the Clay Park drug product with its reference listed drug.

The issue of retention samples will be addressed by the Division of Bioequivalence.

/S/

Mary M. Fanning, MD, PhD
Associate Director for Medical Affairs
Office of Generic Drugs

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-774

BIOEQUIVALENCE REVIEW

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # : 75-774 SPONSOR : Clay-Park Labs, Inc.

DRUG AND DOSAGE FORM : **Ammonium Lactate Cream**

STRENGTH(S) : **12%**

TYPES OF STUDIES : Clinical Endpoint

CLINICAL STUDY SITE(S) : See Review

STUDY SUMMARY : N/A

DISSOLUTION : N/A

DSI INSPECTION STATUS

Inspection needed: YES	Inspection status: COMPLETE	Inspection results: ACCEPTABLE
First Generic _____ New facility __X___ For cause _____ Other _____		

REVIEWER : (Mary Fanning, M.D.)

INITIAL : /S/ DATE : 7/20/01

REVIEWER : (Krista M. Scardina, Pharm.D.)

INITIAL : /S/ DATE : 7/19/01

DEPUTY DIRECTOR: (Rabindra Patnaik, Ph.D.)

INITIAL: /S/ DATE: 7/19/2001

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : /S/ DATE : 7/20/01

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Ammonium Lactate Cream, 12%
ANDA# 75-774
Krista M. Scardina

Clay-Park Labs, Inc.
Submission date: July 3, 2001

Review of a Response to a DSI Report

Background

The Division of Scientific Investigation (DSI) has completed their inspection and submitted their report on July 3, 2001. Dr. Mary Fanning has reviewed issues regarding protocol deviations, and has found the study to be acceptable. Dr. Fanning has deferred the issued of failure to retain reserve drug samples to the Division of Bioequivalence (DBE).

According the DSI report submitted to the DBE, Clinics #4 and #18 did not retain reserve samples as intended by the regulations (21 CFR 320.63). Clay-Park has responded to the 483 findings on May 28, 2001. Clay-Park believes the retained samples were randomized in accordance with the regulations. Clay-Park provided information that the retained samples were randomly selected prior to the study by a third, impartial party, ——————————— who performed the blinding and randomization of the clinical supplies. The ——— , one of the clinical testing facilities, stated that the retained samples were randomly selected and stored by ——— before shipping the drug to clinical testing sites. The retained samples were not selected by the sponsor. The ——— stated that for future bioequivalence studies, they agree to comply with the Agency's policy regarding the retention of samples.

Comments

The sponsor believes that they have complied with the regulations regarding retention samples according to their interpretation. However, after receiving the 483 for failure to properly retain the samples, the sponsor became aware of their misinterpretation and have provided adequate information documenting the flow of drug supplies throughout the study. They have also agreed to comply with the Agency's policy in future studies. Therefore, the bioequivalence study should be acceptable to The DBE.

Recommendation

1. Bioequivalence data as submitted by the firm are acceptable.

2. The firm's explanation and documentation of the flow of study drugs are acceptable.

3. The firm should be advised that when conducting future studies, it is of utmost importance that the firm complies with Agency's regulation regarding retention of study drugs as described in 21 CFR Sections 320.38 and 320.63.

Krista M. Scardina, Pharm.D.
Division of Bioequivalence
Project Manager, Review Branch i

7/19/01

Concur (S) Date: 7/19/01
Lizzie Sanchez, Pharm.D.
Special Assistant to the Director, Division of Bioequivalence

Concur (S) Date: 7/20/01
Dale P. Conner, Pharm. D.
Director, Division of Bioequivalene

V: firmsam/claypark/ltrs&rev/75-774.bio.dsi

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: #75-774 APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Ammonium Lactate Cream, 12%

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

Please be advised that when conducting future studies, it is of utmost importance to comply with the Agency's regulations regarding retention of study drugs as described in 21 CFR 320.38 and 320.63.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon 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,

/S/

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

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-774 APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Ammonium Lactate Cream, 12%

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 revision after review of the entire application, upon 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,

/S/

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

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: #75-774 APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Ammonium Lactate Cream, 12%

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

Please be advised that when conducting future studies, it is of utmost importance to comply with the Agency's regulations regarding retention of study drugs as described in 21 CFR 320.38 and 320.63.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon 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,

/S/

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:

75-774

ADMINISTRATIVE DOCUMENTS

FAX COVER SHEET

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland

To: Cindy Edwards

Phone: _____ Fax: 318-960-0111

From: Pat Burns Block

Phone: (301) 827-5845 Fax: (301) 594-0183

Number of Pages: 2
(Including Cover Sheet)

Comments: Comments from the Division of Bioequivalence follow.

Expired the Red Today.

/S/

APPROVAL PACKAGE SUMMARY FOR 75-774

ANDA: 75-774

FIRM: Clay-park labs, Inc.

DRUG: Ammonium Lactate

DOSAGE: Cream

STRENGTH: 12%

CGMP STATEMENT/EIR UPDATE STATUS: EER is acceptable 12/10/01.

BIO STUDY/BIOEQUIVALENCE STATUS: Bio is satisfactory 7/20/01.

METHODS VALIDATION: The analytical methods are suitable for regulatory analysis.

STABILITY: The firm has provided satisfactory 3 months accelerated stability data at 40°C±2°C/75%±5%RH and 24 months at 25°C±2°C/60%±5%RH. The firm requests 24 months expiration date.

LABELING REVIEW STATUS: Labeling is satisfactory 4/25/02

STERILIZATION VALIDATION: N/A

BATCH SIZES: The firm has provided the master formula and manufacturing process for proposed production batch size ——. Also included exhibit Batch size of —— (Lot #AI563). The firm will be using the same drug substance manufacture, same process, and same equipment.

COMMENTS: The application is approvable.

/S/

REVIEWER: Nashed E. Nashed, Ph.D. DATE: 1/16/02 4/30/02

/S/ 4/30/02

SUPERVISOR: James M. Farr DATE: 2/6/02

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-774

CORRESPONDENCE

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

April 17, 2002

Sarah Ho, Project Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room,
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMEND
N/AF

LABELING AMENDMENT
SUBMITTED BY FAX – HARD COPY TO FOLLOW

RE: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Ho:

Clay-Park Labs, Inc. hereby submits this Labeling Amendment to update the labeling for ANDA # 75-774 for Ammonium Lactate Cream, 12%, based on the FDA-approved template (see **Attachment 1**) for Ammonium Lactate Cream, 12%. The template was provided by the Division of Labeling on April 17, 2002 via e-mail in order to address the Waxman-Hatch Market Exclusively for the innovator's product.

The labeling has been revised accordingly. Twelve (12) copies in the final printed form of the revised labeling for Ammonium Lactate Cream, 12% are presented in **Attachment 2**.

Pursuant to 21 CFR 314.94 (a) (8) (iv), an annotated side-by-side comparison between Clay-Park Labs, Inc.'s revised labeling and the labeling submitted previously by Clay-Park Labs, Inc. in ANDA # 75-774 is provided in **Attachment 3**.

Should you have any comments or require any further clarifications on this amendment, please contact the undersigned as follows:

Telephone: 718-960-9976 **Fax: 718-960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

RECEIVED
APR 1 8 2002
OGD / CDER

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

CERTIFICATION

This is to certify that the field copy of the Labeling Amendment to ANDA #75-774 for Ammonium Lactate Lotion, 12% is a true copy of the original submission to the FDA. The field copy has been forwarded to local New York District Office for their reference.

Candis Edwards
Director of Regulatory Affairs
Clay-Park Labs, Inc.

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

December 5, 2001

Sarah Ho, Project Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

N/AM

MINOR AMENDMENT

Re: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Ho:

Pursuant to 21 CFR 314.120 (a) (1), Clay-Park Labs, Inc. (CPL) hereby submits a Minor Amendment to ANDA # 75-774 for Ammonium Lactate Cream, 12%, in response to the deficiency letter dated July 31, 2001**(see Attachment 1)** and the teleconference held on November 30, 2001 between CPL and OGD representatives.

This Minor Amendment addresses the following:

Update cGMP Compliance Status of CPL's Facility

On October 1-5, 9-12,15-17, 24, 26, 2001, the NY District Office conducted a re-inspection of CPL's facility. As the result of the re-inspection, the facility and controls used for the manufacture, processing, packaging and holding of drug products were determined to be in compliance with the cGMP regulations. The cGMP certification for CPL's facility is provided in **Attachment 2**.

Revised Impurity Limit for Total [redacted] in the Finished Product and Stability Testing of Ammonium Lactate Cream, 12% from NMT [redacted] to NMT [redacted]

A teleconference between CPL and OGD representatives was held on November 30, 2001 to discuss the impurity limit for Total [redacted]. It was agreed that the impurity limit for Total [redacted] in finished product and stability testing of Ammonium Lactate Cream, 12%, would be revised from **NMT** [redacted] **to NMT** [redacted], based on the following scientific rationale:

- The approved limit for Total [redacted]s (Total [redacted], in [redacted]s DMF for Ammonium Lactate, drug substance is NMT [redacted] **(See Attachment 3)**
- **Table 1** presents a summary of [redacted] release results for the % Total [redacted], [redacted] in [redacted] batches of drug substance. The results range from [redacted] % **(See Attachment 3).**
- **Table 2** provides a summary of the results of % Total [redacted] (Total [redacted], from finished product testing of the submission batch, Lot # AI563 and the three (3) process validation batches, Lot #s VA107, VA108 and VA109. Table 2 also includes data generated by [redacted]. (MFR.), and CPL for the specific lots of active drug substance used to manufacture the finished products. **(See Attachment 3).** The data presented in **Table 2** demonstrates that the concentration of Total [redacted] ranges from [redacted]

The data presented in **Table 1 and Table 2** demonstrate that the % Total [redacted] in the finished product is contributed from the drug substance. Therefore, the impurity limit for Total [redacted] in the drug product will be revised from NMT [redacted] to NMT [redacted], to reflect the limit in the drug substance. Additionally, the stability limit for % Total [redacted] is being revised from NMT [redacted] to NMT [redacted] **Attachment 4** provides the revised finished product and stability test monographs to reflect the changes described herein.

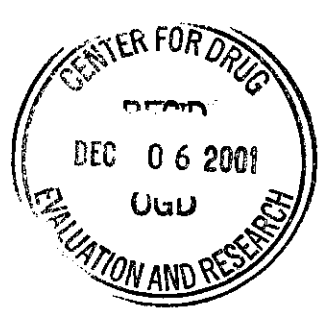
Please note that in the original ANDA, Clay-Park Labs, Inc. asked for approval of [redacted], respectively. Since [redacted] has been out of business as of April 2000, Clay-Park Labs, Inc.'s intent is to use only [redacted] as the [redacted]. The DMF authorization letter and cGMP certification letter from [redacted], is presented in **Attachment 5.**

Should you have any comments or require any further clarification on this amendment, please contact the undersigned as follows:

Telephone (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs



CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

September 13, 2001

Patricia Beers-Block, Approval Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP

SUBMITTED BY FAX
MINOR AMENDMENT

Re: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Beers-Block:

Pursuant to 21 CFR 314.120. (a) (1) and in reference to the Unapprovable Letter dated July 31, 2001 **(See Attached)**, Clay-Park Labs, Inc. hereby submits a Minor Amendment to ANDA # 75-774 for Ammonium Lactate Cream, 12%.

On July 31, 2001 Clay-Park Labs, Inc. received an Unapprovable Letter to ANDA for Ammonium Lactate Cream, 12%, which states the following:

"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 Prescription (Rx) drug product comply with current good manufacturing practices (CGMP) regulations.

Our conclusion is based upon the findings revealed during a recent inspection of Clay-Park Labs, Inc., Bronx, New York from July 6 – August 10, 2000 by representatives of the United States Food and Drug Administration. Upon review of these reports and the inspectional observations noted during this inspection, we have received a recommendation from our Division of Manufacturing and Product Quality (DMPQ), Office of Compliance, to withhold approval of your abbreviated application."

CENTER FOR DRUG
NOV 14 2001

/S/ 11/9/01

Clay-Park Labs, Inc. underwent an FDA inspection on 10/1 – 5, 9 –12, 15 – 17, 24, 26/ 2001, and the facility and controls used for, the manufacture, processing, packaging or holding of the Prescription (Rx) drug product complies with the current good manufacturing practice (cGMP) regulations. Therefore, we respectfully request that the Agency approve ANDA # 75-774 for Ammonium Lactate Cream, 12%.

Should you have any comments or require any further clarification on this amendment, please contact the undersigned as follows:

Telephone (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

Enclosure: Attachment 1

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

September 6, 2001

NEW CORRES
NC
Acknowledged
/S/
9/14/01

Patricia Beers-Block, Approval Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

INFORMATIONAL AMENDMENT

Re: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Beers-Block:

Pursuant to 21 CFR 314.60 (a), Clay-Park Labs, Inc. hereby submits an Informational Amendment to ANDA # 75-774 for Ammonium Lactate Cream, 12% to update the ANDA file, regarding our retest policy for inactive ingredients.

As described on page 2108 (Attachment 1) in Section VIII (3) of the original ANDA, Clay-Park Labs, Inc., previously had a three year retest policy for inactive ingredients. We received comments regarding the retest policy on pending ANDA applications from various review chemists, requesting a change in the retest policy for inactive ingredients.

We conferred with the District Office, and have revised the retest policy for inactive ingredients from three (3) years to one (1) year to meet the current Industry standards.

CENTER FOR DRUG
SEP 10 2001
EVALUATION AND RESEARCH

Should you have any comments or require any further clarification on this amendment, please contact the undersigned as follows:

Telephone (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

Enclosure: Attachment 1
cc: Joseph Famulare
Director, Division of Manufacturing and Product Quality – HFD 320

Richard Trainor
Compliance Officer, FDA District Office

ANDA 75-774

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

JUL 31 2001

Dear Madam:

This is in reference to your abbreviated new drug application dated December 29, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ammonium Lactate Cream, 12%.

Reference is also made to your amendments dated February 1 and June 28, 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 Prescription (Rx) drug product comply with current good manufacturing practice (CGMP) regulations.

Our conclusion is based upon the findings revealed during a recent inspection of Clay-Park Laboratories, Inc, Bronx, New York from July 6 - August 10, 2000 by representatives of the United States Food and Drug Administration. Upon review of these reports and the inspectional observations noted during this inspection, we have received a recommendation 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.

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, and includes a statement from a

responsible corporate officials certifying that the 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,

/S/

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

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

June 28, 2001

Patricia Beers-Block
Approvals Manager, Branch Chief
Office of Generic Drugs, CDER
Food and Drug Administration
Document Control Room
Metro Park North II, HFD-617
7500 Standish Place, Room 150
Rockville, MD 20855

ORIG AMENDMENT

N/A

FRL

INFORMATIONAL AMENDMENT

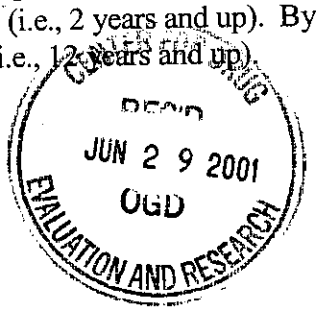
Re: ANDA # 75-774 FOR AMMONIUM LACTATE CREAM, 12%

Dear Ms. Beers-Block:

Clay-Park Labs, Inc. hereby submits this correspondence to update the labeling for ANDA # 75-774 for Ammonium Lactate Cream, 12%, based on the approved labeling revisions for the reference listed drug, Lac-Hydrin® 12% (ammonium lactate cream) Cream manufactured by Bristol-Myers Squibb.

Pursuant to 21 CFR 314.94 (a) (8) (iv), an annotated side-by-side comparison between Clay-Park Labs, Inc.'s revised labeling, and the Innovator's approved labeling is provided in this correspondence.

Please note, that Clay-Park Labs, Inc.'s revised labeling does not include the indication for children under two (2) years old, since Bristol-Myers Squibb has been granted a three (3) year period of exclusivity under the Hatch-Waxman amendments, which will expire on August 25, 2003. The exclusivity has been granted for an expanded pediatric indication, which allows for the treatment of ichthyosis vulgaris and xerosis in pediatric patients as young as two (2) years old. As a result, Bristol Myers Squibb revised its labeling section on Pediatric Use (i.e., 2 years and up). By contrast, Clay-Park Labs, Inc.'s Pediatric Use section remains the same (i.e., 12 years and up).



The following documents are included in this correspondence:

Attachment 1	Clay-Park Labs, Inc.'s revised labeling in the final printed form
Attachment 2	Copy of Clay-Park Labs, Inc.'s labeling submitted in the original application (for reference only)
Attachment 3	Innovator's approved labeling
Attachment 4	Annotated Side-by-Side Comparison Between Clay-Park Labs, Inc.'s Revised Labeling, and Innovator's Approved Labeling
Attachment 5	Tabulated Side-by-Side Comparison Between Clay-Park Labs, Inc.'s Revised Labeling, Innovator's Approved Labeling and Clay-Park Labs, Inc.'s Labeling Submitted in the Original Application

Should you have any questions or require any further clarifications, please contact the undersigned as follows:

Telephone: 718-960-9976 **Fax: 718-960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

February 1, 2001

ORIG AMENDMENT
N/AM

Elaine Hu, Project Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room,
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT

RE: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Hu:

In reference to the deficiency letter dated December 14, 2000 (**Attachment** 1) on our abbreviated new drug application for Ammonium Lactate Cream, 12%, ANDA # 75-774, Clay-Park Labs, Inc. hereby submits the deficiency response for the Chemistry Manufacturing and Control section, designated as a Minor Amendment.

Should you have any comments or require any further clarifications on this amendment, please contact the undersigned as follows:

Telephone: 718-960-9976 **Fax: 718-960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
FEB - 2 2001
OGD

/S/

1 copy
MB

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

December 14, 2000

Krista Scardina
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-615
7500 Standish Place, Room 150
Rockville, MD 20855

NEW CORRESP

Re: Ammonium Lactate Cream, 12%, ANDA # 75-774

Information Amendment

Dear Ms. Scardina:

As per our telephone conversation dated November 14, 2000, please find a SAS data set as you requested, which is included with this correspondence.

Should you have any questions, please call the undersigned as follows:

Tel: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

Enclosure: (1) computer disc

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
DEC 15 2000
OGD

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

October 5, 2000

Elaine Hu, Project Manager
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room,
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT
N/Am1

MINOR AMENDMENT

RE: ANDA # 75-774 Ammonium Lactate Cream, 12%

Dear Ms. Hu:

In reference to the deficiency letter dated September 11, 2000 (**Attachment 1**) on our abbreviated new drug application for Ammonium Lactate Cream, 12%, ANDA # 75-774, Clay-Park Labs, Inc. hereby submits the deficiency response for Chemistry and Labeling sections, designated as a Minor Amendment.

Should you have any comments or require any further clarifications on this amendment, please contact the undersigned as follows:

Telephone: 718-960-9976 **Fax: 718-960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
OCT 16 2000
OGD

10-6-00

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

September 20, 2000

Elaine Hu
Office of Generic Drugs
CDER/FDA
Document Control Room – Room 150
Metro Park North II
7500 Standish place
Rockville, MD 20855

NDA ORIG AMENDMENT
N/AA

INFORMATIONAL AMENDMENT

Re: ANDA # 75-774 Ammonium Lactate Cream, 12% - Additional Information on Inactive Ingredient

Dear Ms. Hu:

Pursuant to 21 CFR 314.96 (a), Clay Park Labs, Inc. (CPL) hereby submits additional information to support the concentration of the inactive ingredient, [redacted] (Glyceryl Monostearate/ PEG 100 Stearate at a [redacted] ratio), in the Ammonium Lactate Cream, 12% (ANDA 75-774) formulation.

This additional information consists of a reverse engineering study report, which describes the determination of Glyceryl Monostearate and PEG 100 Stearate in the innovator's formulations of Lac-Hydrin® 12% Cream and Lac-Hydrin® 12% Lotion and in CPL's formulations of Ammonium Lactate Cream, 12% and Ammonium Lactate lotion, 12%.

The results of the study presented in the report demonstrate that the concentration of Glyceryl Monostearate in the innovator's cream formulation is [redacted] and in the innovator's lotion formulation is [redacted] The data also demonstrate that the concentration of PEG 100 Stearate in the innovator's lotion formulation is [redacted]. The presence of these ingredients in the innovator's product at the concentrations determined above supports CPL's decision to include [redacted] at a concentration of [redacted]

As per a conversation with Nasser Mahmud, we are providing an additional copy of the report so that the review of this data can be coordinated such that it will be reviewed simultaneously with the Pharm/Tox safety data on [redacted] previously submitted on March 16, 2000.

We hope that this information will resolve the question of the concentration of Glyceryl Monostearate/ PEG 100 Stearate that has been used in a previously approved topical drug product.

We are also requesting confirmation as to whether or not the original NDA files were reviewed by the Agency in order to determine the allowable range of Glyceryl Monostearate/ PEG 100 Stearate.

We appreciate your assistance in resolving this issue.

Should you have any comments or require further information please contact the undersigned as follows:

Telephone: 718-960-9976 **Fax: 718-960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

cc. Nasser Mahmud

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

NEW CORRESP
NC

February 24, 2000

Paras Patel
Office of Generic Drugs, CDER
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place – Room 150
Rockville, MD 20855

Re: Correspondence To ANDA # 75-774 for Ammonium Lactate Cream, 12% to Complete ANDA File

Submitted by Fax – Hard Copy to Follow

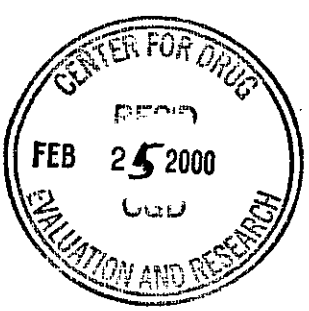
Dear Mr. Patel:

As per a telephone request from Paras Patel, on February 23,1999, Clay-Park Labs, Inc. hereby submits the following information to complete the file for Ammonium Lactate Cream, 12%, ANDA # 75-774:

1) Three (3) complete copies of Section XVII - Analytical Methods – Included with hard copy

2) Attachment 1

   Revised Exclusivity Statement, which acknowledges that at the time of the submission of this application, there was still unexpired pediatric exclusivity as listed in the Orange Book. Additionally, please note that we submitted page 0013 of the hard copy of the original application in error. This page contains patent and exclusivity information from the Electronic Orange Book for NDA # 019927, which is not relevant to this application.



3) Attachment 2

[ ]

4) Attachment 3

Side by Side Package Insert Comparison.

5) We acknowledge FDA's receipt of the correct Form FDA 3454 - CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS originally submitted on 2/11/00 as correspondence to the ANDA file.

We anticipate that the submission of this information will complete this ANDA so that it will be accepted by the Agency or filing. This also certifies that concurrently with the filing of this correspondence, a true copy of this correspondence was sent to our local district office.

Should you have any comments, or require any further clarification, please contact the undersigned as follows:

Telephone: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

V 2.1

pora

ANDA 75-774

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

FEB 29 2000

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated December 29, 1999, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Ammonium Lactate Cream, 12%.

Reference is also made to the telephone conversation dated February 23, 2000 and to your correspondence dated February 24, 2000.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(2) for the following reasons:

The concentration of the inactive ingredient ——— in your proposed product exceeds the maximum concentration of this inactive ingredient previously approved by the Agency. FDA will consider the inactive ingredients or composition of a drug product unsafe and refuse to approve an ANDA under 21 CFR 314.127(a)(8)(i) if, on the basis of information available to the agency, there is a reasonable basis to conclude that one or more of the inactive ingredients of the proposed drug or its composition raise serious questions of safety. Examples of the changes that may raise serious questions of safety include, but are not limited to the following: a change in the composition to include a significantly greater content of an inactive ingredient than previously approved by the agency [21 CFR 314.127(a)(8)(i)]. Please provide additional justification to demonstrate safety of the inactive ingredient ——— such as examples of approved drug products administered by the same route of administration which contain this inactive ingredient in the same concentration range.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Paras Patel
Project Manager
(301) 827-5862

Sincerely yours,

/s/

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

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

February 15, 2000

NEW CORRESP
NC

Harvey Greenberg
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-615
7500 Standish Place, Room 150
Rockville, MD 20855

Re: Ammonium Lactate Cream, 12%, ANDA # 75-774

Dear Mr. Greenberg:

As per our telephone conversation on February 14, 2000, Clay-Park Labs, Inc. is hereby resubmitting the two correspondences dated February 3, 2000 and February 11, 2000, which were submitted to the Agency to update the ANDA file for Ammonium Lactate Cream, 12%, ANDA # 75-774.

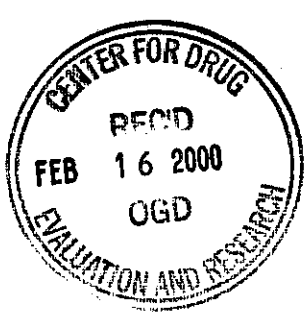
Should you have any questions, please call the undersigned as follows:

Tel: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

Enclosure (2)



CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

February 3, 2000

NEW CORRESP

NC

Douglas Sporn
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855

N 75-774

CORRESPONDENCE TO ANDA FOR AMMONIUM LACTATE CREAM, 12%

RE: ANDA for Ammonium Lactate Cream, 12%

Dear Mr. Sporn,

Clay-Park Labs, Inc. submitted an original Abbreviated New Drug Application (ANDA) for Ammonium Lactate Cream, 12% in the hard copy format on December 29, 1999 and the electronic format on February 1, 2000. During the data entry in Entry Validation Application (EVA) for the electronic submission discrepancies were noted. They have been corrected in the electronic submission document (ESD) and referenced in the companion document.

Clay-Park Labs, Inc. is hereby submitting the corrections to the following discrepancies to update the hard copy ANDA for Ammonium Lactate Cream, 12%:

1. On page 27 of the hard copy, Clay-Park Labs, Inc.'s drug product was incorrectly referred to as Ammonium Lactate Cream USP, 12% in the first line under proposed labeling. The correct name is **Ammonium Lactate Cream, 12%.**

2. On page 1925 of the hard copy, typographical discrepancies were noted in Table 4 as follows:
   - [redacted]

Table 4 has been revised to reflect the changes and is presented in Attachment #1.

3. On page 2053 of the hard copy, typographical discrepancies were made in transcribing the results for Magnesium Aluminum Silicate Type IIA ——— NF, Lot #112085 as follows:
   - Under "Identification" the result should read ***1.495A** not *1495A.
   - Under "Microbial Limits – Total Aerobic Microbial Count", the result should read **<10 cfu/g** not < 10 cfu/µg.

   The revised Certificate of Analysis is presented in Attachment #2.

4. On page 2220 of the hard copy, the result for "Microbial Limit Tests - Total Aerobic Microbial Count" was incorrectly reported as <100 cfu/g in the Certificate of Analysis for Ammonium Lactate Cream, 12 %, Lot #AI563 Bulk Product. The correct result is **<10 cfu/g** and is presented in the revised Certificate of Analysis (See Attachment #3).

5. On pages 2450 through 2452, in the Certificates of Analysis for Ammonium Lactate Cream, 12% - Placebo, Lot #AI564 Finished Product, the statement under "Comments" section was incorrect. The revised Certificates of Analysis with the correct statement under "Comments" is presented in Attachment #4.

6. On page 2520 of the hard copy, the title should read **Assay Chromatograms for Impurities in Ammonium Lactate Cream, 12% - Placebo, Lot #AI564 Finished Product**. The revised title page is presented in Attachment #5.

7. On page 2528 of the hard copy, the title should read **Assay Chromatograms for Lactic Acid in Ammonium Lactate Cream, 12% - Placebo, Lot #AI564 Finished Product**. The revised title page is presented in Attachment #6.

Should you have any questions, please contact the undersigned at the following numbers:

Telephone: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

NEW CORRESP
NC

February 11, 2000

N75-774

Douglas Sporn
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855

CORRESPONDENCE TO UPDATE ANDA FOR AMMONIUM LACTATE CREAM, 12%

Re: Financial Disclosure Form for Ammonium Lactate Cream, 12%

Dear Mr. Sporn:

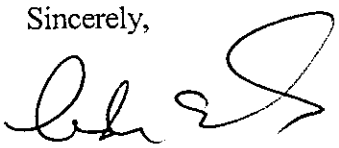
Clay-Park Labs, Inc. submitted an original Abbreviated New Drug Application (ANDA) for Ammonium Lactate Cream, 12% in the hard copy format on December 29, 1999, which included FDA Form 3455 (Disclosure: Financial Interests and Arrangements of Clinical Investigators). Subsequently, we received a correspondence from Agency for another application, where Clay-Park Labs, Inc. was advised to include Form FDA 3454 (Certification: Finanacial Interest and Arrangements of Clinical Investigators) instead of Form FDA 3455, since we did not enter into any financial arrangements with the clinical investigators, as described in the final rule published on February 2, 1998 pertaining to Financial Disclosure.

Based on this, Clay-Park Labs, Inc. is hereby submitting the appropriate form, FDA Form 3454 for all the investigators included in the clincal study entitled "A Double-Blind, Randomized, Parallel, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and clinical equivalence of a Generic Ammonium Lactate Cream, 12% vs Lac-Hydrin® 12% Cream in Patients with Moderate to Severe Ichthyosis Vulgaris." to update the ANDA for Ammonium Lactate Cream, 12%.

Should you have any questions, please call the undersigned as follows:

Tel: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,



Candis Edwards
Director of Regulatory Affairs

Enclosure (1)

CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

February 1, 2000

Douglas Sporn
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855

75-774
NEW CORRESP
NC

Re: Electronic Submission for Ammonium Lactate Cream, 12%, ANDA

Dear Mr. Sporn:

In support of the ANDA for Ammonium Lactate Cream, 12%, hard copy, we are hereby submitting two copies of the electronic submission of the Chemistry, Manufacturing and Control (CMC) section. The CMC electronic submission includes the following files, which are contained on one (1) diskette:

File Name	Document
Cpl0001.003	CMC ESD File
Cpl0001.1gc	Log File
Cpl0001.004	Companion Document including Table of Contents

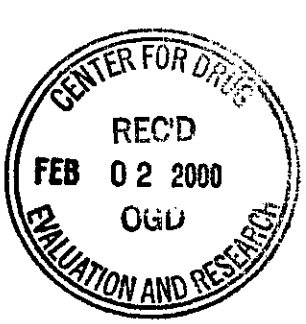
Clay-Park Labs, Inc. hereby submits the CMC electronic submission in the diskettes, which are contained in the blue (Archive Copy) jacket, Form FDA 2626. The written declaration statement is also included in this submission.

Should you have any questions, please contact the undersigned as follows:

Telephone: (718) 960-9976 **Fax: (718) 960-0111**

Sincerely,

Candis Edwards
Director of Regulatory Affairs



CLAY-PARK LABS, INC.

AGIS GROUP

1700 BATHGATE AVE. BRONX, NY 10457 (718)901-2800

December 29, 1999

Douglas Sporn
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855

Re: ANDA for Ammonium Lactate Cream, 12%

Dear Mr. Sporn:

Clay-Park Labs, Inc. hereby submits an original abbreviated new drug application (ANDA) in hard copy format to be followed by electronic format, to seek approval to market Ammonium Lactate Cream, 12% that is bioequivalent to the listed drug, Lac-Hydrin® 12% (ammonium lactate cream) Cream, manufactured by Westwood-Squibb Pharmaceuticals Inc. pursuant to NDA # 020508.

This ANDA consists of eight (8) volumes. Clay-Park Labs, Inc. is filing an archival copy (in blue folders) of the ANDA that contains all the information required in the ANDA and a technical review copy (in red folders) that contains all the information in the archival copy with the exception of the bioequivalence section (VI). A separate copy of the bioequivalence section is provided in orange folders.

This also certifies that, concurrently with the filing of this ANDA, a true copy of the technical sections of the ANDA (including a copy of the 356h form and a certification that the contents are a true copy of those filed with the Office of Generic Drugs) was sent to our local district office. This "field copy" is contained in burgundy folders.

For more detailed information on the organization of this ANDA, please refer to the "Executive Summary" attached after the field copy certification statement.

Clay-Park Labs, Inc. will submit CMC ESD electronic submission (diskettes) for Ammonium Lactate Cream, 12% as new correspondence within the 30 day grace period.

Should you have any comments or require any further clarification on this ANDA, please contact the undersigned as follows:

Telephone: (718) 960-9976 **Fax: (718) 960-0111**

Thank you for your prompt handling of this submission.

Sincerely,

Candis Edwards
Director of Regulatory Affairs