

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-570

ADMINISTRATIVE DOCUMENTS

TELEPHONE MEMO

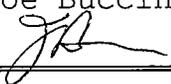
To: Candis Edwards, Clay-Park Labs Inc.
CC: ANDA ~~75-570~~ (for Ammonium Lactate Lotion, 12%)
From: Sandra T. Middleton
Date: March 12, 1999
Subject: Additional time for response to RTF letter

Ms. Edwards requested additional time to respond to the February 17, 1999 RTF letter. I informed her that one additional month would be granted (until April 17, 1999).

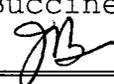
FROM THE DESK OF...
SAUNDRA T. MIDDLETON
PROJECT MANAGER
CDER\FDA\OGD\DLPS
7500 STANDISH PLACE
ROCKVILLE MD 20855

301-827-5862

RECORD OF TELEPHONE CONVERSATION/MEETING

<p>The US Agent set up this t-con with the DMF holder in order to clarify deficiencies in the Aug 3, 1999 fax transmission.</p> <p>The firm questions and the Branch's response are attached.</p> <p>Cc: ANDA 75570 T-con Binder</p> <p>V:\FIRMSAM\CLAYPARK\TELECONS\75570.00 2.doc</p>	DATE October 7, 1999
	ANDA NUMBER 75-570
	DMF NUMBER _____
	TELECON
	INITIATED by DMF Holder
	PRODUCT NAME Ammonium Lactate
	FIRM NAME Clay Park: US Agent _____ DMF Holder
	NAMES Candace Edwards: CP _____ _____ Liang Li Huang: FDA Joe Buccine: FDA
	TELEPHONE NUMBER 3 Way
SIGNATURE Joe Buccine  10/20/99	

RECORD OF TELEPHONE CONVERSATION/MEETING

<p>Reference is made to the firm's fax dated 9/27/99 (attached). In that communication, the firm asked questions regarding the deficiency letter dated 9/14/99.</p> <p>After consulting with the review chemist, Dr. Liang Lii Huang, the firm was provided the attached comments.</p> <p>Cc: ANDA 75570</p> <p>V:\FIRMSAM\CLAYPARK\TELECONS\75570.003.doc</p>	DATE October , 1999
	ANDA NUMBER 75-570
	TELECON
	INITIATED by FDA
	PRODUCT NAME Ammonium Lactate
	FIRM NAME Clay Park
	NAMES Candace Edwards
	TELEPHONE NUMBER
	SIGNATURE Joe Buccine  10/20/99

75-570

FILE

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

6.1

DATE: 9/22/03

TO: C.T. Viswanathan, Ph.D.
Associate Director, Division of Scientific Investigations
MPN I, HFD-48

THROUGH: Dale P. Conner, Pharm. D. Dena R. Hixon MD 9/22/03
Director, Division of Bioequivalence, HFD-650

FROM: DBE/GBIB Liaison
Division of Bioequivalence, Office of Generic Drugs, HFD-617, MPN II

SUBJECT: Biopharmaceutics Compliance Program 7348.001
Request for Inspection

References:

ANDA#	<u>75-570</u>	contact: <u>Candis Edwards</u>	Vice President of Regulatory Affairs.
Product	<u>Ammonium Lactate Lotion, 12%</u>		
Sponsor	<u>Clay - park Labs, Inc</u>		
(full address, phone, fax, contact)	<u>1700 Bathoate Avenue</u>		
	<u>Bronx, NY 10457</u>	<u>(718) 960-9976 FAX: (718) 960-0111</u>	
Submission Date	<u>4/22/02</u>		

Priority B

- A (highest) = ready for approval, outstanding issues
- B = Bio review complete, pending chemistry
- C (routine) = Bio under review

Due Date 12/22/03

**APPEARS THIS WAY
ON ORIGINAL**

I. Studies

Study #1

Number

ANDA 75-570 PROTOCOL # CPL-101

Title

A Double-Blind, Randomized, Parallel-Group, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Clinical Equivalence of a Genetic Ammonium Lactate Lotion 12% vs. Lac-Hydro 12% (Ammonium Lactate)

Clinical Site

(full address, phone, fax)

Lotion in subjects with moderate to severe Ichthyosis Vulgaris
Site # 8

Investigator/Contact

Analytical Site

(full address, phone, fax)

Investigator/Contact
Analytical Method

Study #2

Number

#17

Title

Clinical Site

(full address, phone, fax)

Investigator/Contact

Analytical Site

(full address, phone, fax)

Investigator/Contact
Analytical Method

APPEARS THIS WAY ON ORIGINAL

Study #3

Number

#25

Title

Clinical Site

(full address, phone, fax)

Investigator/Contact

Analytical Site

(full address, phone, fax)

Investigator/Contact
Analytical Method

APPEARS THIS WAY ON ORIGINAL

1. Reason for Inspection Request

- Not inspected in the last three years
 For Cause/Violative history
 New Site
 Other

COMMENTS:

The person submitted investigator's site information only up to #16.
Investigator's information for sites #17-25 are NOT available
please see enclosed document for the clinical report.

2. Bio-study Status

- Study under review
 Study review completed
 study incomplete pending additional information from sponsor
 study unacceptable with questionable data pending inspection verification
 study acceptable pending satisfactory inspection results
 Other:

**APPEARS THIS WAY
ON ORIGINAL**

CC:

HFD-617 (DBE/GBIB Liaison)
HFD-48 (Viswanathan)
HFD-600 (Bio Reviewer) Carol Kim
HFD-600 (PM) Krista Scardina
HFD-630 (ANDA# 75-570)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-570

CORRESPONDENCE



CLAY-PARK LABS, INC.

AP AGIS GROUP

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

January 27, 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

RTF
C. Helquist
2/8/99

Re: ANDA for Ammonium Lactate Lotion, 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 Lotion, 12% that is bioequivalent to the listed drug, Lac-Hydrin® 12% (ammonium lactate) Lotion, manufactured by Westwood-Squibb Pharmaceuticals Inc. pursuant to NDA # 019155.

This ANDA consists of ten volumes. Clay-Park Labs, Inc. is filling 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 "Executive Summary - Organization of the ANDA" attached after the Certification Statement".

Clay-Park Labs, Inc. will submit CMC electronic submission ESD for Ammonium Lactate Lotion, 12% within the 45 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

RECEIVED

JAN 28 1999

GEN DRUGS



CLAY-PARK LABS, INC.

AGIS GROUP

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

CERTIFICATION

This is to certify that the field copy (third copy) of the ANDA 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 1/25/99

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

**APPEARS THIS WAY
ON ORIGINAL**

ANDA 75-570

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

FEB 17 1999

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) dated January 27, 1999, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Ammonium Lactate Lotion, 12%.

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)(3) for the following reasons:

It appears that your proposed formulation contains an inactive ingredient, Fragrance _____, that has not been approved in a drug product for human use by the same route of administration [21 CFR 314.127(a)(8)(ii)]. According to the regulation, there is reasonable basis to conclude that the inactive ingredient in your proposed product may raise safety questions because of the lack of information that you have provided regarding its use. The Office of Generic Drugs (OGD) will not file this application as an ANDA since new inactive ingredients must be the subject of a new drug application. Please provide additional information to support the safety of the use of this inactive ingredient in your proposed drug product. The information to demonstrate safety should include, but is not limited to, examples of approved drug products administered by the same route of administration which contains the same inactive ingredient within the same concentration range.

Please note that DMF authorization and composition alone is not sufficient data to prove safety. If you choose to provide the composition instead of pharmacology toxicology data, you must provide supporting data showing that **each** component and composition was used in an approved drug product.

Form FDA 356h submitted in the archival copy of this application lacks an original signature. Please submit this form with an original signature.

You have failed to provide an English translation of your Certificate of Analysis (COA) for Fragrance. Please provide an english translation per 21 CFR 314.50(g)(2).

Your blank master batch records fail to include master packaging records. Packaging records and reconciliation records are also considered part of the batch records. Please be aware that a batch is not considered processed until it has been completely packaged. Please provide the blank master packaging records.

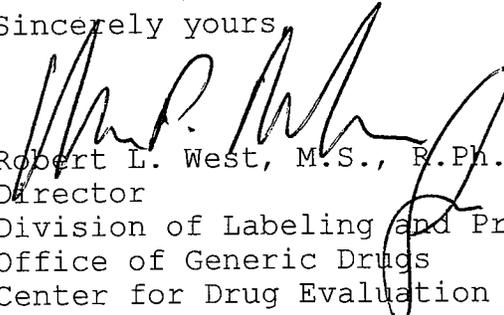
Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

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:

Carol Holquist
Project Manager
(301) 827-5862

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



CLAY-PARK LABS, INC.

AGIS GROUP

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

April 7, 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

NEW CORRESP

NC

Re: Electronic Submission for Ammonium Lactate Lotion, 12%, ANDA # 75-570

Dear Mr. Sporn :

In support of ANDA # 75-570 for Ammonium Lactate Lotion, 12%, hard copy, we are hereby submitting two copies of the electronic submission of the Chemistry, Manufacturing and Control (CMC) section as follows:

Diskette: CMC ESD Files CPL9901.003 and CPL9901.lgc; Companion Document "CPL9901.004" and text contained in the final printed labeling, "CPL9901.Labeling".

In the original paper ANDA for Ammonium Lactate Lotion, 12%, submitted to FDA on January 27, 1999, Clay-Park Labs, Inc. committed to submit the CMC electronic submission within the 45 day grace period. However Clay-Park Labs, Inc. received a refusal to file letter dated February 17, 1999 from the FDA and postponed the electronic submission until all the issues were resolved.

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. Clay-Park Labs, Inc. certifies that the CMC data contained in the electronic submission is identical to that contained in the hard copy.

Additionally, Clay-Park Labs, Inc. is submitting a packaging specification monograph # _____ for _____ white snap top cap which was referenced but not included, in section XIV (2) of the original paper application.

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

RECEIVED

APR 12 1999

GENERIC DRUGS

ANDA 75-570

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

APR 20 1999

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.

Reference is also made to our "Refuse to File" letter dated February 17, 1999 and your amendments dated March 18 and March 26, 1999.

NAME OF DRUG: Ammonium Lactate Lotion, 12%

DATE OF APPLICATION: January 27, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: March 29, 1999

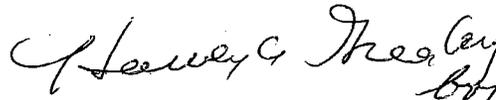
We will correspond with you further after we have had the opportunity to review your application.

Please identify any communications concerning this application with the 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



September 16, 1999

Mary Fanning, M.D.
Associate Director for Medical Affairs
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

NDA ORIG AMENDMENT

N/AB

Re: Telephone Amendment to ANDA # 75-570 for Ammonium Lactate Lotion, 12%

Dear Dr. Fanning:

Following our telephone conversations on September 7 and September 13, 1999, we are providing you with the additional information you requested:

1. A data diskette for clinical study No. 951317 was sent to Harvey Greenberg on March 26, 1999. It is our understanding that this diskette is now in your possession.
2. The randomization list for protocol No. 951317 is included in the final study report, Appendix 1.4, pages 220-236 of the ANDA. For your convenience, enclosed please find an additional copy of the randomization summary.
3. Enclosed is the list of patients used in the Per Protocol statistical analyses. A total of 159 subjects were eligible for the Per Protocol therapeutic equivalence and efficacy analyses of the treatment and post-treatment period. These Per Protocol statistical analyses included only patients who had efficacy assessments for visits 3 and 4, and excluded Protocol Violators as defined and listed in Section 4.1.1.1 Protocol Violations, of the Integrated Clinical and Statistical Report, page 0110 of the ANDA.

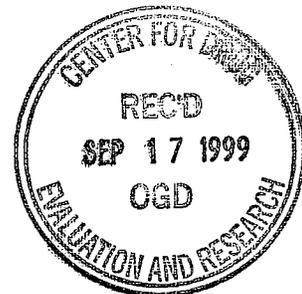
Should you have any further questions, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Candis Edwards
Director of Regulatory Affairs





November 19, 1999

Joseph Buccine
Food and Drug Administration
Office of Generic Drugs, CDER
Division of Labeling and Program Support
Document Control Room
Metro Park North 2, HFD-623
7500 Standish Place
Rockville, MD 20855

NDP DRUG AMENDMENT

FPL
AC
enter
Final review noted:
A/Bolan
5/31/02

MAJOR AMENDMENT

RE: ANDA # 75-570 Ammonium Lactate Lotion, 12%

Dear Mr. Buccine:

In reference to the deficiency letter dated September 14, 1999 (**Attachment 1**) on our abbreviated new drug application for Ammonium Lactate Lotion, 12%, ANDA # 75-570, Clay-Park Labs, Inc. hereby submits the deficiency response for Chemistry and Labeling sections, designated as a Major Amendment.

Clay-Park Labs, Inc. will submit CMC ESD electronic submission (diskettes) for the major amendment to ANDA # 75-570 for Ammonium Lactate Lotion, 12% as a new correspondence within the 30 day grace period.

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





CLAY-PARK LABS, INC.

AGIS GROUP

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

December 23, 1999

ORIG AMENDMENT

N/A/C

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: Electronic Submission for Ammonium Lactate Lotion,
12%, ANDA # 75-570, Major Amendment**

Dear Mr. Sporn:

In reference to the FDA deficiency letter dated September 14, 1999 on our abbreviated new drug application for Ammonium Lactate Lotion, 12%, ANDA # 75-570, Clay-Park Labs, Inc. hereby submits the deficiency response for Chemistry and Labeling sections designated as a Major Amendment, in the electronic version. The CMC electronic submission includes the following files, which are contained on one (1) diskette:

File Name	Document
Cp19906.003	CMC ESD File
Cp19906.1gc	Log File
Cp19906.004	Companion Document

Clay-Park Labs, Inc. hereby submits the CMC electronic submission for the major amendment in two (2) diskettes, which are contained in the blue (Archive Copy) jacket, Form FDA 2626. The written declaration statement is also included in this submission.

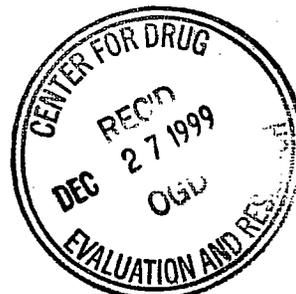
Should you have any questions, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Candis Edwards
Director of Regulatory Affairs



BIOEQUIVALENCY AMENDMENT [FEB - 8 2000]

ANDA 75-570

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: Jennifer Fan

PROJECT MANAGER (301) 827-5847

Dear Ms. Edwards:

This facsimile is in reference to the bioequivalency data submitted on March 26, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ammonium Lactate Lotion, 12%.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached ____ pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all 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. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

X:\new\ogdadmin\glossary\biofax.frm

FEB -8 2000

BIOEQUIVALENCY DEFICIENCIES

ANDA: 75-570

APPLICANT: Clay-Park Labs, Inc.

DRUG PRODUCT: Ammonium Lactate Lotion, 12%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. An equivalence comparison is only valid if the reference treatment is effective against placebo in the trial. The test drug must also be effective against placebo in the trial. You did not analyze the reference drug against placebo and conducted a pooled analysis of the actives versus placebo. A separate analysis of the efficacy of test versus placebo and reference versus placebo should be conducted.
2. You changed the efficacy criteria for the efficacy analysis of Test versus Reference when the original analysis failed and did not change the equivalence criteria. Such a post-hoc change is not desirable. The criteria for evaluating efficacy and equivalence should be the same.
3. When these analyses were done, neither the Clay-Park test product nor the Lac-Hydrin reference product was superior to the placebo treatment.
4. The efficacy test should be carried out at $\alpha = 0.05$ for a two-sided test or $\alpha = 0.025$ for a one-sided test, not at an alpha level of 0.05 for a one-sided test.
5. The sample size calculation was not done correctly in that the previous points were not considered. In addition, the sample size was calculated for testing the difference between 2 treatments of the means of a variable with a 10-point scale while the statistical comparison was to be done on the difference in success rates of two treatments.

**APPEARS THIS WAY
ON ORIGINAL**

6. The sample size requirements were re-calculated for the efficacy testing for 15% difference using chi-square test and for equivalence testing of 15% limit using two one-sided tests (Farrington and Manning's asymptotic test procedure). The required sample size would be the maximum of the two sizes. The sample size required for the placebo group is between 100 and 170 depending on the assumed true response proportion of the placebo group. The sample size of each of the active treatment groups is between 112 and 159 depending on the true response proportion of the reference treatment group assuming that the response proportion of the reference treatment group ranges from 60% to 75%. It shows that the study was not designed with appropriate sample sizes to demonstrate the efficacy of test and reference over placebo or the equivalence of the test and reference treatments of dichotomized outcome.
7. The Per Protocol Population is used to evaluate equivalence. This population should exclude subjects who had protocol violations as well as those who were out of the visit window for the bioequivalence primary endpoint.
8. Using Wald's Test with Continuity Correction or the Farrington and Manning approach, the test and reference product do not meet bioequivalence criteria regardless of how the Per Protocol Population was defined.

Sincerely yours,



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

ANDA 75-570

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

MAR 13 2000

Dear Madam:

This letter is in reference to your abbreviated new drug application dated January 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ammonium Lactate Lotion, 12%.

Reference is also made to your amendments dated September 16, November 19, and December 23, 1999.

This application is not approvable under section 505 of the Act for the following reason:

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)(ii) 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)(ii)]. 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.

The Office of Generic Drugs will suspend any further review of this application until an amendment containing complete information and data necessary to support your chosen plan of action is submitted to the Agency.

The file is now closed. It is required that an action described under 21 CFR §314.120 and 21 CFR §314.96 be taken, which will either amend or withdraw this application. Should it be decided to amend this application, the amendment should respond to all cited deficiencies stated above and/or to those presented in previous letters. In the event that reformulation of the test product is needed to meet the agency's bioequivalence requirements, revised chemistry, manufacturing, controls and labeling information should also be included in the amendment. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered as a Major Amendment and should be so designated in your cover letter. The cover letter should clearly state what information is being provided in the submission (i.e., Chemistry, Bioequivalence, Labeling). If there is substantial disagreement with our reasons for not approving this application, a hearing request can be submitted.

If you have any questions, please contact Elaine Hu at (301) 827-5848. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,



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



October 2, 2000

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

NEW CORRESP

nc

NAI
Elaine Hu
10/17/00

RE: ANDA # 75-570: Ammonium Lactate 12% Lotion

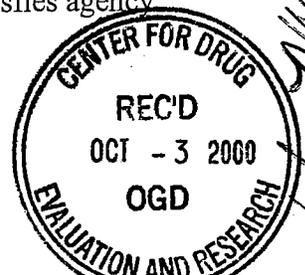
Dear Elaine:

By letter dated March 13, 2000, received by Clay-Park Laboratories, Inc. on March 20, the Office of Generic Drugs informed Clay-Park Labs, Inc. that its ANDA # 75-570 for Ammonium Lactate Lotion, 12% was not approvable. The Agency cited questions regarding the concentration of the inactive ingredient, _____ in Clay-Park Labs, Inc.'s proposed drug product.

As provided in 21 CFR 314.120(a)(5), this letter expresses our intent to amend ANDA # 75-570 at such time as the agency completes its review of an identical question on the safety of the inactive ingredient, _____ raised by the agency – and still pending before the agency – with respect to Clay-Park Labs, Inc.'s submitted ANDA # 75-774 for Ammonium Lactate Cream, 12%.

Specifically, by letter dated February 29, 2000, the FDA expressed its refusal to file Clay-Park Labs, Inc.'s ANDA # 75-774 for Ammonium Lactate Cream, 12%, which had been submitted to the FDA on December 29, 1999. Clay-Park Labs, Inc. replied to that refusal to file letter by correspondence dated March 16, 2000, in which Clay-Park Labs, Inc. submitted additional information supporting the safety of _____ at the proposed concentration level. We are still awaiting the response to the March 16, 2000 submission.

As the file on Clay-Park, Inc.'s ANDA # 75-570 for Ammonium Lactate Lotion, 12% also should reflect, prior to receiving the non-approval letter on the lotion due to the questions on _____, Clay-Park Labs, Inc had also been informed, by FDA communication dated February 8, 2000, that its bioequivalence study for the Lotion was deficient. As provided in 21 CFR 314.120(a)(5), this letter also expresses Clay-Park Labs, Inc.'s intent to amend its application to include a new bioequivalence study on the lotion formulation that satisfies agency requirements.



105700

However, as both the cream and the lotion products use the same concentration of _____, Clay-Park Labs, Inc. is not prepared to initiate any new bioequivalence studies on the Lotion until the inactive ingredient issue is resolved.

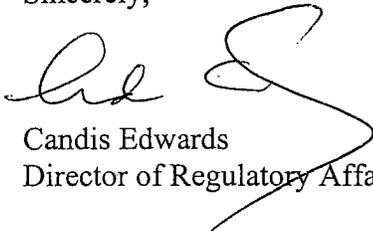
Clay-Park Labs, Inc. understands that the information submitted on March 13, 2000, in response to the refusal letter on its ANDA #75-774 for Ammonium Lactate Cream, 12% is still under review at the agency. Accordingly, because the information submitted in support of the safe use of _____ in Clay-Park Labs, Inc.'s ANDA # 75-774 for Ammonium Lactate Cream, 12% also would support a conclusion relative to the issues raised in the non-approvable letter on the lotion dated March 13, 2000, Clay-Park Labs, Inc. asks that the agency defer any further action on its ANDA # 75-570 for Ammonium Lactate Lotion, 12% until at least a reasonable period of time (estimated to not exceed 180 days) following the receipt by Clay-Park Labs, Inc. of the agency's review of the information submitted in support of _____ with respect to the cream application. During that period, Clay-Park will inform the agency as to its specific plans with respect to amending ANDA #75-570 for Ammonium Lactate Lotion, 12%.

If the office has any questions on this in the interim, please feel free to contact the undersign as follows:

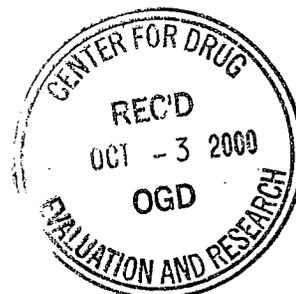
Telephone: (718) 960-9976

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

October 31, 2000

NEW CORRESP

NC

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

**RE: Informational Amendment to ANDA # 75-570 For
Ammonium Lactate Lotion, 12%**

Dear Elaine:

In reference to the Not Approvable Letter dated March 13, and the Bioequivalence Deficiency Letter dated February 8, 2000, to ANDA # 75-570 for Ammonium Lactate Lotion, 12%, Clay Park Labs, Inc. hereby submits this correspondence in order to notify the Agency of our intent to repeat the clinical end point bioequivalence study on Ammonium Lactate Lotion, 12%.

Not Approvable Letter Dated March 13, 2000

On March 13, 2000 Clay-park Labs, Inc. received a "not approvable letter" for Ammonium Lactate Lotion, 12%. The letter stated:

"The concentration of the inactive ingredient _____ in your proposed product exceeds the maximum concentration of this inactive ingredient previously approved by the Agency."

On March 16, 2000 we submitted Safety/ Toxicology data for _____ to ANDA # 75-774 for Ammonium Lactate Cream, 12%, which contained the same concentration of _____ as Ammonium Lactate Lotion, 12%.

As per a telephone conversation with Nasser Mahmud, Branch Chief, Regulatory Support Branch, on October 18, 2000, we were informed that the Safety/ Toxicology data for _____ was accepted by the Agency as sufficient to demonstrate the safety of this ingredient in our cream and lotion formulations. Therefore, we intend to proceed with a repeat clinical end-point bioequivalence study using the formulation for Ammonium Lactate Lotion, 12%, which was submitted in ANDA # 75-570.



Bioequivalence Deficiency Letter Dated February 8, 2000

On February 8, 2000 Clay-Park Labs, Inc. received a Bioequivalence Deficiency Letter for Ammonium Lactate Lotion, 12%. The letter cited various deficiencies in the design and outcome of study, resulting in a failed study.

In the interim, we conducted a clinical end point bio study for ANDA # 75-774 for Ammonium Lactate Cream, 12%, which has the same indication as the lotion. The protocol for the cream study took into account the Agency's Comments from the deficiency letter for the lotion. Additionally the protocol was revised to define a specific test area for the purpose of evaluation of severity of disease and improvement or cure of disease.

On October 26, 2000 we were notified by the Division of Bioequivalence that the design of the clinical end point study conducted on Ammonium Lactate Cream, 12% ANDA # 75-774 was acceptable and that we could use the same study design to conduct the repeat clinical end-point bioequivalence study on Ammonium Lactate Lotion, 12%.

Therefore, this correspondence serves to notify the Agency that it is Clay-Park Labs, Inc.'s intent to initiate a clinical end point bioequivalence study on Ammonium Lactate Lotion, 12%, using the FDA approved study protocol that was used to conduct the study on Ammonium Lactate Cream, 12% (ANDA # 75-774). Upon completion of the study, Clay-Park Labs, Inc. will submit the study results as an Amendment to ANDA # 75-570 for Ammonium Lactate Lotion, 12% in response to the bioequivalence deficiency letter.

CMC Section

Additionally, please note that we received the Chemistry and Labeling Deficiency Letter dated September 14, 1999 for Ammonium Lactate Lotion, 12% (ANDA #75-570). Clay-Park Labs, Inc. submitted a deficiency response designated as a Major Amendment on November 14, 1999.

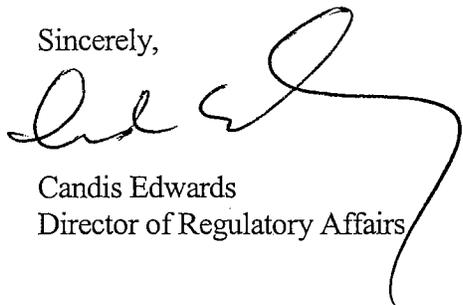
Since this amendment has been on hold as a result of the not approvable letter, we anticipate that the amendment will now receive a timely review so that we can proceed toward with product approval.

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

cc. Nasser Mahmud; Lizzie Sanchez



ANDA 75-570

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

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

MAY 16 2001

Dear Madam:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated January 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ammonium Lactate Lotion, 12%.

We refer you to our "Not Approvable" letter dated March 3, 2000, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

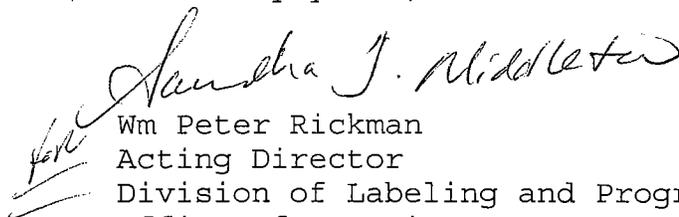
If you have further questions you may contact Sandra T. Middleton, Project Manager, Regulatory Support Branch, at (301) 827-5862.

**APPEARS THIS WAY
ON ORIGINAL**

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

for


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

cc: ANDA 75-570
DUP/Division File
HFD-610/PRickman

Endorsement: *for*

HFD-615/GDavis, Chief, RSB,

S. Middleton

date 5/16/01

HFD-615/SMiddleton, CSO,

S. Middleton

date 5/16/01

Word File

V:\FIRMSAM\CLAYPARK\LTRS&REV\75570.OTH

F/T by EEH 05/16/01

10 DAY LETTER!



CLAY-PARK LABS, INC.



AGIS GROUP

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

*6/21/01
From should
be checked
11/30/01
Starts
S. Middleton*

Open vol

May 23, 2001

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

x-1

SUBMITTED BY FAX

Re: CORRESPONDENCE TO ANDA # 75-570 FOR AMMONIUM LACTATE LOTION, 12%

Dear Ms. Middleton:

In response to the FDA Certified Letter, dated May 16, 2001 (see attached) regarding ANDA # 75-570 for Ammonium Lactate Lotion, 12% and as per our telephone conversation today, Clay-Park Labs, Inc. hereby submits this correspondence in order to notify the Agency of our intent to amend ANDA # 75-570 for Ammonium Lactate Lotion, 12%.

On October 31, 2000, we submitted an informational amendment to ANDA # 75-570 notifying the Agency of our intent to repeat the clinical end-point bioequivalence study on Ammonium Lactate Lotion, 12%. The bioequivalence study on Ammonium Lactate Lotion, 12% was initiated on February 15, 2001, and is ongoing. Upon successful completion of the study, Clay-Park Labs, Inc. will submit the study results and the relevant CMC data in an Amendment to ANDA # 75-570 for Ammonium Lactate Lotion, 12%. The tentative date of submission of the amendment is November 2001.

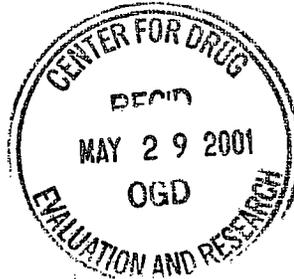
Should you have any questions or require any further clarifications, please contact the undersigned as follows:

Telephone: 718-960-9976

Fax: 718-960-0111

Sincerely,

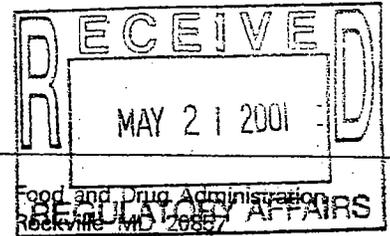
Candis Edwards
Director of Regulatory Affairs





DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDA 75-570



CERTIFIED MAIL-RETURN RECEIPT REQUESTED

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

MAY 16 2001

Dear Madam:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated January 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ammonium Lactate Lotion, 12%.

We refer you to our "Not Approvable" letter dated March 3, 2000, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

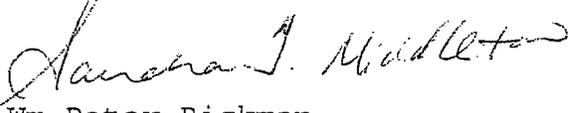
If you have further questions you may contact Sandra T. Middleton, Project Manager, Regulatory Support Branch, at (301) 827-5862.

APPEARS THIS WAY
ON ORIGINAL

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

for 

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

**APPEARS THIS WAY
ON ORIGINAL**



October 12, 2001

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

Saundra Middleton
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation IV
Division of Anti-Infective Drug Products
HFD-520
5600 Fisher Park Lane
Rockville, MD 20857

NEW CORRESP

RECEIVED

OCT 15 2001

MEGA/CDER

Re: Safety Report
Non-Drug Related Serious Adverse Events
Ammonium Lactate Lotion, 12%, ANDA # 75-570

Dear Ms. Middleton:

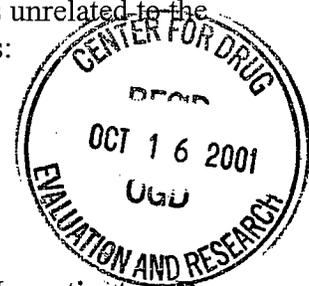
Clay-Park Labs, Inc. hereby reports six (6) non-drug related Serious Adverse Events (SAEs) for five (5) subjects (see Attachment 1 for SAE Summary) that occurred during the clinical study CPL-101, entitled "A Double-Blind, Randomized, Parallel-Group, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Clinical Equivalence of a Generic Ammonium Lactate Lotion, 12% vs. Lac-Hydrin 12% (Ammonium Lactate) Lotion in Subjects with Moderate to Severe Ichthyosis Vulgaris" as follows:

Non-Drug Related Serious Adverse Event for Subject No. 323, Site 06, Investigator: Dr.

Subject number 323, a 62 year old female, was enrolled in the study on February 20, 2001. On [redacted], subject had a elective angioplasty surgery. The subject had a history of angina starting in 1997, and was being treated with Nitroglycerine. Subject came in for her Week 4 visit on March 22, 2001. Her angina is markedly improved.

Dr. [redacted], Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 2, for copies of the following documents:

- Correspondence notifying IRB of the SAE
FDA Form 3500A
Adverse Events page from the subject's case report form
Letter from Principal Investigator to CRO



Non-Drug Related Serious Adverse Event for Subject No. 566, Site 06, Investigator: Dr.

Subject number 566, a 86 year old female, was enrolled in the study on April 19, 2001. Subject was admitted to [redacted] Hospital on [redacted] with congestive heart failure (left

ventricular failure). Subject's history included hypertension since year 2000, which being treated with Zestril. Subject was discharged from the hospital on _____. Follow-up report on May 29, 2001 indicates that the subject has clinical evidence of left ventricular failure. Subject had improved fully and has been advised to follow up with her primary physician.

Dr. _____ Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 3, for copies of the following documents:

- Correspondence notifying IRB of the SAE
- FDA Form 3500A
- Follow-up FDA Form 3500A
- Adverse Events page from the subject's case report form
- Letter from Principal Investigator to CRO

Non-Drug Related Serious Adverse Event for Subject No. 235, Site 17, Investigator: Dr. _____

Subject number 235, a 59 year old male, was enrolled in the study on March 29, 2001. Subject had two (2) SAEs:

1. On _____, subject had outpatient surgery for a left wrist fracture. Subject was supposed to leave the hospital on the same day but had trouble waking up from the anesthesia and was subsequently admitted for observation. Subject was treated and discharged on _____ and given Percocet and Tylenol # 3.

Dr. _____ Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 4, for copies of the following documents:

- Correspondence notifying IRB of the SAE
 - FDA Form 3500A
 - Follow-up FDA Form 3500A
 - Adverse Events page from the subject's case report form
 - Letter from Principal Investigator to CRO
2. On / _____, subject was taken to the _____ Hospital with a fever of 104.9° F. Subject was diagnosed with pneumonia and hospitalized from _____ to _____ On _____ subject was released in good health.

Dr. _____ Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 4, for copies of the following documents:

- Correspondence notifying IRB of the SAE
- FDA Form 3500A
- Follow-up FDA Form 3500A
- Adverse Events page from the subject's case report form
- Letter from Principal Investigator to CRO

Non-Drug Related Serious Adverse Event for Subject No. 261, Site 18, Investigator: Dr. _____

Subject number 261, a 63 year old male, was enrolled in the study on March 28, 2001. On May 7, 2001 the subject's wife notified the study coordinator that subject has been hospitalized and had surgery performed to repair an abdominal aortic aneurysm on _____. The subject's conditions were stable and improving after surgery.

Dr. _____, Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 5, for copies of the following documents:

- Correspondence notifying IRB of the SAE
- FDA Form 3500A
- Adverse Events page from the subject's case report form
- Letter from study coordinator to CRO
- Follow-up Letter from study coordinator to CRO including copies of previous submission regarding this SAE and hospital discharge summary

Non-Drug Related Serious Adverse Event for Subject No. 400, Site 25, Investigator: Dr. _____

Subject number 400, a 74 year old female, was enrolled in the study on April 10, 2001. On _____ subject went to the local emergency room complaining of dizziness and had been hospitalized from _____ to _____ for worsening hypertension. Subject recently began taking medication after being diagnosed with hypertension on May 7, 2001. This SAE was reported to the study coordinator on June 21, 2001.

Dr. _____, Principal Investigator at the site evaluated this SAE as unrelated to the study medication. See Attachment 6, for copies of the following documents:

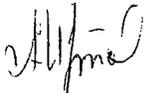
- Correspondence notifying IRB of the SAE
- FDA Form 3500A
- Adverse Events page from the subject's case report form
- Letter from the study coordinator to CRO

Should you have any questions or require any additional information, please call the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,



for
Candis Edwards
Director of Regulatory Affairs



meB

April 22, 2002

Gary Buehler, Director
Food and Drug Administration
OGD-CDER Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room #150
Rockville, MD 20855-2773

ORIG AMENDMENT
AC

**RE: BIOEQUIVALENCE AMENDMENT TO
ANDA # 75-570
AMMONIUM LACTATE LOTION, 12%**

Dear Mr. Buehler:

In reference to the Bioequivalency Deficiency letter dated February 8, 2002 (**Attachment A**), on our abbreviated new drug application for Ammonium Lactate Lotion, 12%, ANDA #75-570, Clay-Park Labs, Inc. hereby submits a deficiency response for the bioequivalency section, designated as a bioequivalency amendment.

The clinical end-point bioequivalency study for Ammonium Lactate Lotion, 12% was repeated and the study results and the relevant CMC data are presented in this Amendment.

Should you require any further information, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Candis Edwards
Director of Regulatory Affairs

RECEIVED

APR 23 2002

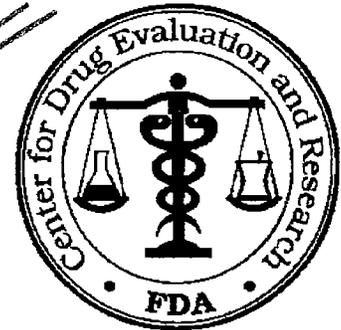
OGD / CDER

MINOR AMENDMENT

ANDA 75-570

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)

JUN 11 2003



APPLICANT: Clay Park Labs, Inc.

TEL: 718-960-9976

ATTN: Candis Edwards

FAX: 718-960-0111

FROM: Thuyanh Vu

PROJECT MANAGER: 301-827-5754

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated January 27, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ammonium Lactate Lotion, 12%.

Reference is also made to your amendment(s) dated: April 22, 2002.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (1 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 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:

CMC comments provided.

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

If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

Redacted 1

Page(s) of trade

secret and /or

confidential

commercial

information



CLAY-PARK LABS, INC.

AP AGIS GROUP

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

July 11, 2003

ORIG AMENDMENT

N/A m

Dr. Rashmikant M. Patel, Director,
Division of Chemistry I
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 #75-570 for Ammonium Lactate Lotion, 12%

Dear Mr. Rashmikant M. Patel:

In reference to the deficiency letter for the Chemistry section dated June 11, 2003 (**Attachment 1**) on our abbreviated new drug application for Ammonium Lactate Lotion, 12%, ANDA #75-570 Clay-Park Labs, Inc. hereby submits the deficiency response for the Chemistry section, designated as a Minor Amendment.

Should you require any further assistance, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Candis Edwards
Vice President, Regulatory Affairs

RECEIVED

JUL 14 2003

OGD/CDER

NEW
7-24-03



CLAY-PARK LABS, INC.

AGIS GROUP

July 14, 2003

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

Dr. Rashmikant M. Patel, Director
Division of Chemistry I
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP

NC
6/14/03

**SUBMITTED BY FAX
HARD COPY TO FOLLOW**

INFORMATIONAL AMENDMENT

Re: ANDA # 75-570 for Ammonium Lactate Lotion, 12%

Dear Dr. Patel:

Clay-Park Labs, Inc. hereby submits this Informational Amendment to correct the monograph included in the Minor Amendment submitted in error on July 11, 2003 for ANDA # 75-570, for Ammonium Lactate Lotion, 12%, in response to FDA Deficiency letter dated June 11, 2003.

The enclosed current Stability Product Monograph dated June 19, 2003, Edition 03-01, replaces the monograph dated April 18, 2002, Edition 02-01, on page 06 to 17 of the Minor Amendment.

Should you require any further assistance, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Candis Edwards
Vice President of Regulatory Affairs

Cc: Ann Vu, Project Manager (FDA)

RECEIVED
JUL 15 2003
OGD/CDER

7/14
8-5-03



October 15, 2003

Ms. Carol Y. Kim, Pharm. D.,
Clinical Reviewer
Food and Drug Administration
Office of Generic Drugs
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

N/AB

Bioequivalence Telephone Amendment

Re: ANDA # 75-570 Ammonium Lactate Lotion, 12%

Dear Ms. Kim:

Pursuant to our telephone conversation on October 8, 2003 regarding the Agency's request for information (See **Attachment 1**), Clay-Park Labs, Inc. hereby submits this Telephone Amendment to ANDA # 75-570 for Ammonium Lactate Lotion, 12%. This amendment consists of two (2) volumes with the following information:

1. New SAS data set with the variables requested by the Agency (**Attachment 2**)
2. Copy of the Case Report Form for the requested patients (**Attachment 3**)
3. Study site summary information for sites #.17-25 which was originally submitted to the FDA in one volume. We are hereby replacing this volume, which contains pages 1397 – 1978 of the original application (**Attachment 4**). The information requested on Dr _____ role and credentials (site #25) are included in pages 1915 and 1926-1928 respectively.

Please find enclosed an archival copy of the Amendment in a blue binder with the SAS data set in electronic format, and a reviewer's copy of the Amendment in an orange binder.

RECEIVED

OCT 16 2003

OGD/CDEH

Should you require further assistance, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

Cathleen Gabney
for Candis Edwards
Vice President of Regulatory Affairs

**APPEARS THIS WAY
ON ORIGINAL**



December 19, 2003

ORIG AMENDMENT
(N/A M)

Ms. Ann Vu
Division of Chemistry I
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

**SUBMITTED BY FAX
HARD COPY TO FOLLOW
TELEPHONE AMENDMENT**

Re: ANDA # 75-570 for Ammonium Lactate Lotion, 12%

Dear Ms. Vu:

This is in response to our telephone conversation on December 18, 2003 regarding the Stability Product Test Monograph and Stability Data Summary Report for Ammonium Lactate Lotion, 12% ANDA # 75-570, with respect to the specification of NMT — % for _____ in the impurity profile.

The Stability Product Test Monograph in the Minor Amendment submitted on July 11, 2003 had a specification for _____ of NMT —%. However, we realized the error and submitted a Telephone Amendment on July 14, 2003 which included a revised Stability Product Test Monograph with the new specification for _____ of NMT —%. As per our discussion, page # 11 of this monograph was missing from your files.

Subsequently the Stability Product Test Monograph was further revised on October 16, 2003 for clarification purposes. In order to update the ANDA, Clay-Park Labs, Inc. hereby submits a Telephone Amendment which provides the current Stability Product Test Monograph (see **Attachment 1**). Also please find enclosed the revised Post Approval Stability Protocols (see **Attachment 2**) and Stability Data Summary Reports (see **Attachment 3**), which have been updated to incorporate the change in the specification for _____

RECEIVED

DEC 22 2003

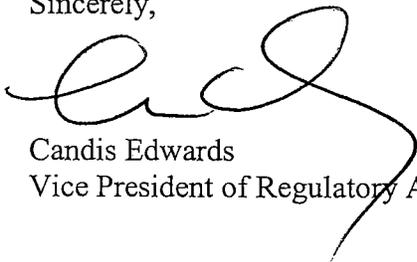
OGD / CDER

Should you require any further assistance, please contact the undersigned as follows:

Telephone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

A handwritten signature in black ink, appearing to read 'Candis Edwards', with a long, sweeping underline that extends to the right and then curves back down.

Candis Edwards
Vice President of Regulatory Affairs

**APPEARS THIS WAY
ON ORIGINAL**

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

FDA

To: Candis Edwards

Phone: 718 960 9976

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From: Krista Scardina

Phone: (301) 827-5845

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Number of Pages: 3
(Including Cover Sheet)



Comments:

Please note: This is for your information only.
No response is needed.

Thanks.

Krista

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ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL,
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BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75-570

APPLICANT:Clay Park labs. Inc.

DRUG PRODUCT: Ammonium Lactate Lotion, 12%

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

The data submitted to ANDA 75-570, using the primary endpoint of clinical success (mean Overall Disease Severity score of 2 or less on a scale of 0 to 9) rate at the end of treatment (Week 4), are adequate to demonstrate bioequivalence of Clay Park Labs. Inc.'s Ammonium Lactate Lotion, 12%, with the reference listed drug, Westwood-Squibb's Lac-Hydrin[®] Lotion, 12%. Both active treatments demonstrated superiority over the placebo arm at Week 4.

1. For bioequivalence studies with clinical endpoints involving treatment of ichthyosis vulgaris, the OGD has previously recommended that both generic and reference products should be superior to placebo at both weeks 4 and 6 (in the ITT population) to demonstrate that the study is sufficiently sensitive to discern a difference between products. However, bioequivalence is evaluated only at week 4. The week 6 endpoint does not contribute to the evaluation of bioequivalence. Therefore, for this and future studies of ammonium lactate products for treatment of ichthyosis vulgaris, the OGD will consider the endpoint at week 4 only.
2. It is your responsibility to assure that the clinical sites for all future BE studies comply with the requirements for retention of study drugs for each shipment as per 21 CFR 320.38 and 320.63. If you fail to comply with the Agency's regulation in any subsequent study, the study may be found unacceptable and a new bioequivalence study may be requested. Please refer to "Handling and Retention of BA and BE Testing Samples", posted 8/20/02 for details.

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,

A handwritten signature in cursive script, appearing to read "Dale P. Conner".

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

**APPEARS THIS WAY
ON ORIGINAL**



CLAY-PARK LABS, INC.

ORIGINAL



AGIS GROUP

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

7.1

June 21, 2004

Ms. Beverly Weitzman
Division of Labeling and Program Support
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

MC

**TELEPHONE AMENDMENT
SUBMITTED BY FAX
HARD COPY TO FOLLOW**

Re: ANDA #75-570 Ammonium Lactate Lotion, 12%

Dear Ms. Weitzman:

As per our discussion with the Agency today, in reference to our application for Ammonium Lactate Lotion, 12%, ANDA # 75-570, Clay-Park Labs, Inc. hereby commits to revise its package insert in accordance with the innovator's recently revised labeling within the next six (6) months or by the next printing of the insert, whichever occurs first.

These revisions include the addition of a Geriatric Use statement in the Precautions Section and revised wording in the Carcinogenesis, Mutagenesis, Impairment of Fertility Section.

Should you require any further information, please contact the undersigned as follows:

Phone: (718) 960-9976

Fax: (718) 960-0111

Sincerely,

C. Edwards
for Candis Edwards

Vice President of Regulatory Affairs

Cc: Ann Vu, Project Manager

RECEIVED
JUN 22 2004
OGD / CDER