CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-570

LABELING REVIEW(S)

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

ANDA Number: 75-570 Date of Submission: January 27, 1999

Applicant's Name: Clay Park Labs, Inc.

Established Name: Ammonium Lactate Lotion, 12% (Lactic Acid)

Labeling Deficiencies:

CONTAINER/INSERT (225 g and 400 g)

1. Revise the "See package..." statement to read, "Usual Dosage: See package...".

2. Include the storage temperature range in degrees Fahrenheit.

3. GENERAL COMMENTS

   a. Include the footnotes and references to be in accord with the March 27, 1986, approved labeling for this product.

   b. Revise so that there is consistency in your labeling format (i.e., section headings in bold lettering, subsection headings not in bold lettering [e.g., **Precautions** - General]).

   c. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone as on labels or the title of the package insert.

4. CLINICAL PHARMACOLOGY

   Delete the left parenthesis preceding "α-hydroxy" in the 3rd sentence of the second paragraph.

5. PRECAUTIONS

   a. Carcinogenesis, Mutagenesis, Impairment of Fertility

      Delete " [redacted] " from the first sentence.

b. Pregnancy (Category C)

i. The subsection heading should read, *Pregnancy.* Teratogenic Effects. Pregnancy Category C

ii. Delete " [redacted] " throughout this subsection.

c. Nursing Mothers

i. Revise so that this subsection is one paragraph rather than two.

ii. Delete " [redacted] ".

d. Pediatric Use

Delete " [redacted] ".

6. OVERDOSAGE

a. Delete " [redacted] ".

b. The official abbreviation for milliliter is "mL".

7. References

See GENERAL COMMENT (a).

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

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

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

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

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

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling (continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			

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

NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:

1. Labeling review based on the labeling for the reference listed drug (Lac Hydrin 12% Lotion – Westwood-Squibb; revised January 1992; approved March 27,1986).

2. Packaging
   The RLD packages its product in 225 and 400 g bottles.

   The applicant is proposing to package its product in 225 g and 400 g white, HDPE plastic bottles. The caps are white, threaded, and hinged with snap tops.

All pages are accounted for in this labeling document. A numbering error occurred.

("For the record" items skip from 2 to 4. Error is carried over to next labeling review, as well.)

4. Labeling

Clay-Park plans to use a fix-a-form label that combines the product container label and package insert into one physical unit that adheres to the face of the bottle. The insert has a reseal feature.

It appears that Lac-Hydrin has more current container labels that include a warning. However, since the patient is directed to look at the package insert, which includes this information in the PRECAUTIONS section, Clay-Park will not be asked to change their label.

A print out of the electronic version of the PDR does not include footnotes or the references. However, since the approved 1986 labeling does include this information, Clay-Park has been asked to include it also.

5. Inactive Ingredients

There does not appear to be a discrepancy in inactives between the DESCRIPTION section of the insert labeling and the C&C statements.

6. USP Issues

Not a USP item

RLD - Store at CRT 15-30°C (59-86°F).

ANDA - Have been asked to include the range in Fahrenheit.

7. Bioequivalence Issues - Pending

8. Patent/Exclusivity Issues - None Pending

Date of Review: August 23, 1999

Date of Submission: January 27, 1999

Primary Reviewer: [signature] Date: 8/23/99

Team Leader: [signature] Date: 8/25/1999

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cc: ANDA: 75-570
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Review

3.1

APPROVAL SUMMARY

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

ANDA Number: 75-570

Date of Submission: November 19, 1999

Applicant's Name: Clay Park Labs, Inc.

Established Name: Ammonium Lactate Lotion, 12%

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

- Do you have 12 Final Printed Labels and Labeling? Yes
- CONTAINER/INSERT (225 g and 400 g) - Satisfactory in final print as of November 19, 1999 submission. [V3.1; Attachment 19]

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Lac-Hydrin Lotion 12%
- NDA Number: 19-155
- NDA Drug Name: Ammonium Lactate Lotion, 12%
- NDA Firm: Bristol Myers Squibb Pharmaceutical Research, Inc.
- Date of Approval of NDA Insert: March 27,1986
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labeling: Side-by-side comparison
- Revisions needed post-approval: No
- Patent/Exclusivity: Refer to chart below:

Patent Data – NDA 19-155

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	None	III	None

Exclusivity-Data – NDA 19-155

Code	Reference	Expiration	Labeling Impact
	NONE		

Labeling has changed s Supplement 019 provide for a geriatric use subsection, and Supplement 020 provide for Revised wording to the carcinogenesis, Mutagenesis r Impairment ? Fertility section of the label. The firm provided A commitment letter to revise their package insert to add "geriatric "section & revise the "carcinogenesis, mutagenesis, & Impairment & fertility" section. Beverly Waltmon 6/21/04

Firm submitted Telefax Amendment dated June 21, 2004.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		X	
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?		X	
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Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
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Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
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			X

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Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
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NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:

1. **MODELING LABELING**
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2. **PACKAGING**
   The RLD packages its product in 225 and 400 g bottles.

   The applicant is proposing to package its product in 225 g and 400 g white, HDPE plastic bottles. The caps are white, threaded, and hinged with snap tops.

4. **LABELING**
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5. **INACTIVE INGREDIENTS**

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6. **USP ISSUES**
Not a USP item
RLD – Store at CRT 15-30°C (59-86°F).
ANDA – Have been asked to include the range in Fahrenheit.

7. **PATENT/EXCLUSIVITY ISSUES** – None Pending

Date of Review: **Date of Submission: November 19, 1999**

Primary Reviewer: B. Weitzman **Date:** 4/14/03
B. Weitzman

Team Leader: **Date:** 4/21/2003

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Review

APPEARS THIS WAY
ON ORIGINAL