CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 74-489

ADMINISTRATIVE DOCUMENTS

OGD APPROVAL ROUTING SUMMARY

ANDA # 74-489 Applicant Copley Pharmaceutical, Inc
Drug Hydrocortisone Valerate Cream USP, 0.2%
Strength

APPROVAL ☒ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐

REVIEWER:

1. Project Manager Buccine
   Review Support Br III

DRAFT RECEIPT
Date 7/22/98
Initials [illegible]

FINAL ACTION
Date
Initials

Application Summary:
Original Rec'd date 4/28/94
Date Acceptable for Filing 12/18/95
Patent Certification (type) NONE
Date of Office Bio Review 5/29/97
Methods Val. Samples Pending Yes ☐ No ☒
30 Day Clock Start End
Commitment rcd. from Firm Yes ☐ No ☐
First Generic Yes ☒ No ☐

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 6-25-98
Date Patent in effect NONE
Citizens Petition/Legal Case Yes ☐ No ☒
(If YES, attach email from PM to Pet. Coord. notifying of pending approval)
Pediatric Exclusivity Tracking System
Date checked
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

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

2. Div. Dir./Deputy Dir.
   Chemistry Div. (I) or II
   Comments:

Date 7/23/98 Initials [illegible]
Date 7/23/98 Initials [illegible]

CMC section is satisfactory (this is Acting Dep. Dir.) This ANDA is from his Branch

3. Office Level Chem Review (1st Generic Only)
   Chemistry Div. (I) or II
   Comments:

Date 7/23/98 Initials [illegible]
Date 7/27/98 Initials [illegible]

CMC section is satisfactory

4. Pat Beers Block
   Supv., Review Support Branch
   Comments: RLD = NDA #17950

Date 7/27/98 Initials PMBB
Date 7/28/98 Initials PMBB ok

- EER acceptable 6/25/98
- FPL acceptable 2/17/98
- Patent Cert – no pending patents or exclusivity for Westwood-Squibb's Hydrocortisone Valerate Crm.
- Bioequivalence office sign off 5/29/97
- No citizens petitions or law suits info.
- No controlled correspondence
- CMC acceptable (review dtd. 7/23/98; Approval summary dtd. 7/17/98)
- All open correspondence is addressed in the approval letter
- Ped. exclusivity not applicable (no patents / exclusive marketing for #17950)

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

5. Peter Rickman
Supv., Reg. Support Branch
Contains certification Yes ☒ No ☐
(required by the GDEA if sub after 6/1/92)
Paragraph 4 Certification Yes ☐ No ☒
Comments: NDA - 17-950

No patent or exclusivity issues
Office Level Bio 5/29/97
EER acceptable 6/25/98

Date 8/4/98 Initials [illegible] | Date 8/7/98 Initials [illegible]
Determ. of involvement? Yes ☐ No ☒
Pediatric Exclusivity Tracking System
Date Checked N/A
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

1st Generic

6. Jerry Phillips
Dir. Div. Labeling & Prog. Support
Comments:
- EER - Status OK as of 8/11/98
- No Pediatric Exclusivity request; NO ~~Pedi~~ Exclusivity or Patents
- NO C.P or legal cases pending
- Bio acceptable, labeling OK

Satisfactory for 1st generic approval

Date 8/7/98 Initials JP | Date 8/11/98 Initials [illegible]

7. Gordon Johnston
Deputy Director, OGD
Patent Cert - P_4 Yes ☐ No ☒
Pend. Legal Action Yes ☐ No ☒
Comments:

Date _____ Initials _____ | Date 8/11/98 Initials _____
Petition Status None

8. ~~Doug~~ Sporn
Dir., OGD
Comments:

Date _____ Initials _____ | Date _____ Initials _____

Roger Williams, M.D.
Dep.Dir., CDER

Date 8/12/98 Initials [illegible] | Date _____ Initials _____

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

9. Project Manager Joe Baucom
Review Support Branch
Date 8/12/98 Initials [illegible] | Date 8/13/98 Initials [illegible]
_____ Pediatric Exclusivity Tracking System (check just prior to notification to firm)
Applicant notification:
8/13 Time notified of approval by phone 9:15 Time approval letter faxed 8/13/98
FDA Notification:
8/13 Date e-mail message sent to "OGD approvals" account
8/13 Date Approval letter copied to"//cder/drugapp" directory

APPROVAL PACKAGE SUMMARY FOR 74-489

ANDA: 74-489

FIRM: Copley Pharmaceutical Inc.

DRUG: Hydrocortisone Valerate

DOSAGE: Cream

STRENGTH: 0.2%

CGMP STATEMENT/EIR UPDATE STATUS: EER is acceptable 6/25/98

BIO STUDY/BIOEQUIVALENCE STATUS: The bio is acceptable 5/29/97

METHODS VALIDATION: The drug product is compendial

STABILITY: The firm has provided the 18 and 24 months room temperature stability data. The firm propose 18 months expiration date.

LABELING REVIEW STATUS: The labeling is satisfactory 2/13/98

STERILIZATION VALIDATION: N/A

BATCH SIZES: The firm has submitted the master formula and manufacturing instruction for the maximum batch

The firm has provided a copy of the executed batch record lot 679Z02 for The firm will be using the same drug substance The DMF is satisfactory, same equipment and same procedure.

COMMENTS: The Application is Approvable.

/S/

REVIEWER: Nashed E. Nashed, Ph.D. Date: 7/17/98

Supervisor: Paul Schwartz, Ph.D. /S/

X:\NEW\FIRMSAM\COPLEY\LTRS&REV\74-489.SUM

RECORD OF TELEPHONE CONVERSATION

Reference was made to Copley's amendment dated 10/31/97, page 238.

The firm was asked to made the following revision:

Please change your blend uniformity commitment. It should state that if the firm wants to suspend blend uniformity testing, a prior approval supplement will be submitted.

The firm agreed.

A fax will be submitted today, followed by a complete telephone amendment to the file.

cc:
ANDA
T-con Binder

DATE
7/27/98

ANDA NUMBER
74-489

IND NUMBER

TELECON

FDA PARTICIPANTS
Joe Buccine

PRODUCT NAME
Hydrocortisone Valerate

FIRM NAME
Copley Pharmaceuticals

FIRM PARTICIPANTS
Isadoro Nudelman

TELEPHONE NUMBER
(781) 575-7520

SIGNATURE
Joseph Buccine

JB 7/27/98

FIRST GENERIC

Not-Approval Letter or Approval Package

	Date Forwarded	Date Completed
Deputy Director Tier-3 Review Allen Rudman (or Acting Deputy)	Paul is the Acting Dep. Director, But the AWDP was reviewed in his Area	
Division Director Audit Rashmi Patel (or Acting Director)	7/23/98	7/27/98 FGAA Rec'd

RECORD OF TELEPHONE CONVERSATION

Reference was made to Copley's fax dated 4/16/98.

On page 10, requirement 9 for total known and unknown related substances, the stability spec of NMT is too high. Please change this spec to NMT . This spec represents the calculated average of samples taken at the top, middle and bottom of the tube.

The firm agreed.

cc:
ANDA
Div File
T-con Binder

DATE
4/21/98

ANDA NUMBER
74-489

IND NUMBER

TELECON

FDA PARTICIPANTS
Joe Buccine
Nashed Nashed
Paul Schwartz

PRODUCT NAME
Hydrocortisone Valerate

FIRM NAME
Copley Pharmaceuticals

FIRM PARTICIPANTS
Isadoro Nudelman
Helen Milano

TELEPHONE NUMBER
(781) 575-7520

SIGNATURE
Joseph Buccine
JB 4/21/98

for July 15, 1998

Application: **ANDA 74489/000**
Stamp: **26-APR-1994** Regulatory Due:
Applicant: **COPLEY PHARM**
CANTON COMMERCE CENTER
25 JOHN RD
CANTON, MA 02021

Priority:
Org Code: **600**
Action Goal:
District Goal: **26-JUN-1995**
Brand Name:
Established Name: **HYDROCORTISONE VALERATE**
Generic Name:
Dosage Form: **CRM (CREAM)**
Strength: **0.2%**

FDA Contacts: **J. BUCCINE** **(HFD-617)** **301-827-5848** **, Project Manager**

Overall Recommendation:

ACCEPTABLE on 25-JUN-1998 by M. EGAS (HFD-322) 301-594-0095

Establishment: **1221807**
COPLEY PHARMACEUTICAL INC
CANTON COMMERCE CENTER
25 JOHN RD
CANTON, MA 02021

DMF No:
AADA No:

Profile: **OIN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **25-JUN-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Establishment:

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **14-JAN-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE OTHER TESTER**

Establishment:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **14-JAN-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE OTHER TESTER**

Establishment:

DMF No:
AADA No:

30

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 14-JAN-1998
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: DRUG SUBSTANCE MANUFACTURER

Establishment:

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 14-JAN-1998
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE OTHER TESTER

RECORD OF TELEPHONE CONVERSATION

Reference was made to Copley's fax amendment dated 3/16/98.

The firm was asked to made the following revisions:

1. On page 7, please provide the expiration dates of the RLD lots and the dates of the assays.

2. On pages 7-11, recalculate all the levels using the response factor identified in previous converations with Paul Schwartz.

The firm agreed.

cc:
ANDA
T-con Binder

DATE
6/26/98

ANDA NUMBER
74-489

IND NUMBER

TELECON

FDA PARTICIPANTS
Joe Buccine
Paul Schwartz

PRODUCT NAME
Hydrocortisone Valerate

FIRM NAME
Copley Pharmaceuticals

FIRM PARTICIPANTS
Isadoro Nudelman

TELEPHONE NUMBER
(781) 575-7520

SIGNATURE
Joseph Buccine
JB 6/26/98

RECORD OF TELEPHONE CONVERSATION

Reference was made to data contained in the March 17, 1998 submission (p. 15).

The firm was called to clarify degradation variability for he variability occurs between tube #1 and #2 and within top, middle and bottom of each tube.

The sponsor claims that variability is due to the active ingredient in the product being suspended. This variability is also encountered in the brand drug. The sponsor claims that the generic variability is no worse than the brand.

The sponsor postulates that variability in is due to conversion to/from This opinion is being investigated.

The Branch requested the following information:

1. Update on the status of the investigation.

2. Commitment to develop a method that clarifies the variability of

3. Update the stability protocol to state that two tubes are tested at each station.

Copley agrees.

cc:
ANDA
Div File
T-con Binder

4/16
In addition on p. 5:
a. Eliminated "No individual Assay for greater than
b. Replace ≤ spec for Total Impurity (Known + unknown)

status of response requested 4/14/98 JB

DATE
3/27/98

ANDA NUMBER
74-489

IND NUMBER

TELECON

FDA PARTICIPANTS
Joe Buccine
Nashed Nashed
Paul Schwartz

PRODUCT NAME
Hydrocortisone Valerate

FIRM NAME
Copley Pharmaceuticals

FIRM PARTICIPANTS
Isadoro Nudelman
Helen Milano

TELEPHONE NUMBER
(781) 575-7520

SIGNATURE
Joseph Buccine
JB 3/27/98

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The Branch requested the following information:

1. Update on the status of the investigation.

2. Commitment to develop a method that clarifies the variability of

3. Update the stability protocol to state that two tubes are tested at each station.

Copley agrees.

cc:
ANDA
Div File
T-con Binder

DATE
3/27/98

ANDA NUMBER
74-489

IND NUMBER

TELECON

FDA PARTICIPANTS
Joe Buccine
Nashed Nashed
Paul Schwartz

PRODUCT NAME
Hydrocortisone Valerate

FIRM NAME
Copley Pharmaceuticals

FIRM PARTICIPANTS
Isadoro Nudelman
Helen Milano

TELEPHONE NUMBER
(781) 575-7520

SIGNATURE
Joseph Buccine
3/27/98

APPROVAL SUMMARY

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

ANDA Number: 74-489

Date of Submission: October 31, 1997 (Amendment)

Applicant's Name: Copley Pharmaceutical, Inc.

Established Name: Hydrocortisone Valerate Cream USP, 0.2%

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

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (15 g, 45 g, 60 g, and 120 g)
Satisfactory as of October 31, 1997 submission

Carton Labeling: (15 g, 45 g, 60 g, and 120 g)
Satisfactory as of October 31, 1997 submission

Professional Package Insert Labeling:
Satisfactory as of October 31, 1997 submission

Revisions needed post-approval:

PRECAUTIONS "Rx only"

1. General

   Revise the fifth paragraph to use "children" rather than "pediatric patients".

2. Carcinogenesis, Mutagenesis, and Impairment of Fertility

   Revise to delete "and" from the subsection heading.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Westcort Cream, 0.2%

NDA Number: 17-950

NDA Drug Name: Hydrocortisone Valerate Cream USP, 0.2%

NDA Firm: Westwood Pharmaceutical

Date of Approval of NDA Insert and supplement #009:
January 28, 1983

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: 17-950

Basis of Approval for the Carton Labeling: 17-950

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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.	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
PROPRIETARY NAME			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
PACKAGING - The innovator packages in product in 15 g, 45 g, 60 g and 120 g tubes. Copley is proposing to market its product in the same sizes, in designed to meet standards of tamper resistance. (page 980, Section XIV)			
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	

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	
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	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
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	
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.			
Inactive Ingredients: (FTR: List page # in application where inactives are listed) Volume 1.1, page 809			
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	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations) USP - Preserve in well closed containers. NDA - Store below 78°F (26°C) ANDA - Store below 26°C (78°F)			
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	

Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) Pending			
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. None pending.			

FOR THE RECORD:

1. Labeling review based on the listed drug (Westcort Cr., Westwood Pharmaceuticals, Inc., approved 1/28/83.) The side-by-side labeling submitted by Copley revised 1982 and 1990 were used for reviewing the container labels and carton labeling since they were more current than the 1977 labeling approved 3/17/78 available from Drug Information. Although there are minor differences, (e.g., "Store below 26°C (78°F)" instead of "Do not store above 77°F (25°C)"; "For topical use only" instead of "For topical use"), after conferring with J Grace, it was decided to use the information from the more current labeling.

2. This is the first generic for this product.

3. FTR comments are contained within the Labeling Reviewer's Checklist.

Date of Review:
February 13,1998

Date of Submission:
October 31, 1997

Primary Reviewer:
/S/

Date:
2/13/98

Team Leader:
/S/

Date:
2/17/98

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

Date of Review: June 10, 1996

Date of Submission: December 15, 1995

Primary Reviewer: Lillie D. Golson

Secondary Reviewer: Adolph Vezza

ANDA Number: 74-489 **Review Cycle:** #1

Applicant's Name [as seen on 356(h)]:
Copley Pharmaceutical Inc.

Established Name: Hydrocortisone Valerate Cream USP, 0.2%
(NOTE: This is the first generic for this product)

LABELING DEFICIENCIES, WHICH ARE TO BE INCORPORATED WITH THE CHEMISTRY COMMENTS TO THE FIRM:

A. CHEMISTRY DEFICIENCIES

B. LABELING DEFICIENCIES

1. GENERAL COMMENT:

   Delete the terminal zero throughout your labeling when expressing a strength or a concentration (e.g., 2 mg rather than 2.0 mg).

2. CONTAINER (15 g, 45 g, 60 g, and 120 g)

   a. See GENERAL COMMENT

   b. Revise the description statement to read,

      Each gram contains: 2 mg Hydrocortisone valerate in a hydrophylic base composed of white petrolatum...

3. CARTON (15 g, 45 g, 60 g, and 120 g)

   See CONTAINER Comments

4. INSERT

a. DESCRIPTION

Revise paragraph 2 to read,

Each gram of Hydrocortisone Valerate Cream 0.2% contains...

b. PRECAUTIONS

i. Information for Patients

Revise #1 to be one paragraph.

ii. Pregnancy (Category C)

Revise the subheading to read,

Pregnancy: *Teratogenic Effects*, Pregnancy Category C.

iii. Pediatric Use

Revise paragraph one to read, ...a larger skin surface area to body weight ratio.

c. Revise the **Caution** statement to read, ...dispensing without prescription. (delete "a")

Please revise your labels and labeling, as instructed above, and submit in final print. To facilitate review of your 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 latest submission with all the differences annotated and explained. Please note that we reserve the right to request further changes in your labels and or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's 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, page 765	x		
Is this name different than that used in the Orange Book?		x	
Error Prevention Analysis			
PROPRIETARY NAME			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
PACKAGING - The innovator packages in product in 15 g, 45 g, 60 g and 120 g tubes. Copley is proposing to market its product in the same sizes, in (page 980, Section XIV)			
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	
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	
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	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
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	
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.			
Inactive Ingredients: (FTR: List page # in application where inactives are listed) Volume 1.1, page 809			

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	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations) USP - Preserve in well closed containers. NDA - Store below 78°F (26°C) ANDA - Store below 26°C (78°F)			
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	
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) Bio information submitted by firm deemed incomplete in 3/8/95 letter.			
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. None pending.			

FOR THE RECORD:

1. Labeling review based on the listed drug (Westcort Cr., Westwood Pharmaceuticals, Inc., approved 1/28/83.) The side-by-side labeling submitted by Copley revised 1982 and 1990 were used for reviewing the container labels and carton labeling since they were more current than the 1977 labeling approved 3/17/78 available from Drug Information. Although there are minor differences, (e.g., "Store below 26°C (78°F)" instead of "Do not store above 77°F (25°C)"; "For topical use only" instead of "For topical use"), after conferring with J Grace, it was decided to use the information from the more current labeling.

2. This is the first generic for this product.

3. FTR comments are contained within the Labeling Reviewer's Checklist.

M E M O R A N D U M

From: Larry Galvin, Consumer Safety Technician
Division of Bioequivalence

To: ANDA 74-489 -- For the record

Ref.: Response to RF Refusal to File letter

On May 19, 1994 the Office of Generic Drugs issued an RF letter for Hydrocortisone Valerate Cream USP, 0.2% to Copley Pharmaceutical, Inc.

On October 3, 1994 they responded with a bio protocol based on the results of a pilot study. This correspondence was received by the Document Room on October 5, 1994 and was identified as NEW CORRESPONDENCE/BIO and because of its REFUSE TO FILE status, was apparently not properly routed, and therefore fell through a crack and remained unanswered.

Subsequently, on January 25, 1995, the sponsor submitted an amendment to this earlier BIO submission which was forwarded to Margo and then to BIO. It was only when an attempt was made to enter this new document into the MIS that we realized that an earlier document had not been properly recorded.

Upon reviewing the content of these two documents, it was discovered that neither document properly responds, completely, to the RF letter of May 19, 1994.

ANDA Assignment Record

Appl Type/Number: N 074489 Status/Date: PN PENDING REVIEW 26-APR-94
Firm: COPLEY PHARM
Trade Name: USP: Y
HYDROCORTISONE VALERATE

✓ OTC: ___ Dosage Form: CRM Strength: 0.2%

Therapeutic Class: 4020600 CP

Doc Set Type: N 000 Amend/Type: _____ Letter Date: 28-MAR-94
Rec-d Date: 26-APR-94 Acknl. Date: __-___-__
Bio Rev Type: To Bio: __-___-__

		Assigned	Completed
Lbl:	AMP Complete Package	5-13-94	__-___-__
Chm:	RN4 Random II	4-29-94 CP	__-___-__
Bio:	___	__-___-__	__-___-__
Ins:	___	__-___-__	__-___-__
Col:	___	__-___-__	__-___-__
Co2:	___	__-___-__	__-___-__

DESI Drug: _____ Similar or Related: _____

Applicant Manufacturer: Yes ✓ No _____

If No: Name of Mfg: _____

ANDA #_____ Approved: _____ Pending: _____ Same Formulation: _____

Application Complete: Yes ✓ No RF

Application Acceptable: Yes ✓ No RF

If No: Non-Acceptable Letter to Firm: __-___-__

CSO/CST: _____ Date: 5-2-94

505(j)(2)(A)

CParnes
5/3/94
RTF
Does Not Comply
Interim Guide

ANDA CHECKLIST FOR COMPLETENESS AND ACCEPTABILITY OF THE APPLICATION

AADA/ANDA# 74-489

DRUG NAME Hydrocortisone Valerate

DOSAGE FORM Cream USP 0.2% FIRST REVIEW

SUPERVISORY CHEMIST (Schwartz)

RANDOM ASSIGNMENT (Random III)*

*If high potency, 1 mg/dosage unit or less, assign to Branch 2

	YES	NO
Therapeutic Code (4020600 ✓ / Steroidal Skin Products) Comments EC1 ✓ On Cards ✓		
Methods Validation package (3 copies) (✓) Required for Non-USP drugs	3/25/94 4/26/94	
Cover Letter	✓	
Letters of Authorization		
U.S. Agent (If Needed, Countersignature on 356h)		
DMF Referral(s) ok		
356h Form - Completed/Original Signature	✓	
Table of Contents	✓	
Listed Drug/Firm Ortho / Sq. Hill	✓	
AADA Monograph	✓	
Information to show proposed product is the same as the listed product: (i)(a) indications (ii) active ingredient(s) (iii) (a) route (b) dosage form (c) strength (iv) labeling -- side by side comparison - insert:	NA	
container:	✓	
Same Formulation? same qualitative / differs quantitative ~~Not Bioequivalent~~	✓	
(Ophthalmics/Otics/Externals/Parenterals)	✓ the same	
Parenterals: Same Size Container (strength/volume)	- NA	
Petition Required		✓
Debarment Certification pg 4	✓	
List of Convictions	✓	
Third Copy Certification Sent to 805-DD pg 6	✓	
Patent Certification	✓ I	
Use Patent Statement?	NA	
Exclude Use in labeling/indications?	NA	
Exclusivity Addressed (If Applicable)	✓	
Five year exclusivity? *If yes, cannot be filed until expiration or after 4 years if challenged.*	NA	
Labeling: 4 copies of draft (✓) or 12 copies of FPL( )	✓	
Statement re Rx/OTC Status	✓	
Components & Composition (Unit Composition)	✓	
Manufacturing Controls	✓	
Batch Formulation	✓	
Master Production Batch Record for largest batch size intended for production. (No more than 10x pilot batch)	✓	
Certification of GMP. pg 8-13	✓	
Description of Facilities	✓	
Address of Manufacturing Site for Production Batches	✓	
Manufacturing Procedures (Batch Records) 479202	✓	
Package entire exhibit bio batch.		✓
Number(s)/Mfg. Facility 479202 / Cost-MA	✓	
If Sterile product:		
Aseptic Fill ____ Terminal Sterilization ____	NA	

Specifications and Tests for Active Ingredient and Dosage Form		
Source of Active Ingredient	✓	
COA from Manufacturer of Active Ingredient	✓	
Applicant COA	✓	
COA for finished product	✓	
	✓	
Specifications and Tests for Inactive Ingredients		
Source of Inactive Ingredients Identified	✓	
COA from Manufacturer of Inactive Ingredient	✓	
Applicant COA for Inactive Ingredients	✓	
	✓	
Stability Profile Including Stability Data (Use of Stability Indicating Method)	✓	
3 mo. Accelerated Stability Data	12 month LT data on file	
Batch Numbers Listed on Stability Records 679202	✓	
Samples Statement Plus Data	✓	
	✓	
Bioavailability/Bioequivalence	✓	
Study Vasoconstrictor Study	✓	
In Vivo Study/Waiver Request	NA	
Comparative Dissolution Data	✓	
Paragraph IV bio study acceptable for filing	NA	
Date acceptable for filing	NA	
Environmental Impact Analysis	✓	
Compliance Statement	✓	

Reviewing CSO (Blaine Nelson)

Date 5/2/94

Recommendation: File / Refuse to File

Supervisory Concurrence/Date 5/3/94

Duplicate copy sent to Bio:
(Hold if RF and send when acceptable)

Duplicate copy to HFD- 520 **for consult**
Type of Consult: Bio - Vasoconstrictor assay

Micro Consult: Yes ____ No ✓

Revision 10-22-93 bcw/C:\wpfiles\rev.chk

Formulation: Some qualitative
Differs quantitative
Vasoconstrictor assay 4/20/93
Does not comply ☐ intern guide

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE

COPLEY PHARM
25 JOHN RD CANTON COMMERCE CENTER
CANTON MA 02021

ANDA #: N074489

Dear Sir/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 for the following:

NAME OF DRUG:
HYDROCORTISONE VALERATE
Dosage Form: CRM USP Potency: 0.2% USP: Y

DATE OF APPLICATION: 28-MAR-94

DATE OF RECEIPT: 26-APR-94

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

However, in the interim, please submit three additional copies of the analytical methods and descriptive information needed to perform the tests on the samples (both the bulk active ingredient(s) and finished dosage form) and validate the analytical methods. Please do not send samples unless specifically requested to do so. If samples are required for validation, we will inform you where to send them in a separate communication.

If the above methodology is not submitted, the review of the application will be delayed.

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

Sincerely yours,

Schwartz HFD-629
Randolph IR

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Fax 505(j)(2)(A)
4/28/94

ANDA/AADA PROCESSING RECORD

ANDA/AADA NO. 74-489

DATE		INITIALS
4/26/94	DATE RECEIVED BY DOCUMENT ROOM	MCB
4/28/94	DATE RECEIVED BY PROGRAM SUPPORT STAFF	MCB
4/29/94	DATE FORWARDED TO CSO/CSO TECH FOR REVIEW	MCB
5/2/94	DATE FILING REVIEW COMPLETED/FORWARDED FOR SUPERVISORY REVIEW	KR
5/3/94	DATE SENT TO TYPING	OF
_____	DATE TYPING COMPLETED	_____
_____	DATE SENT FOR DIRECTOR'S SIGNATURE	_____
_____	DATE OF OGD SIGNATURE	_____

I N T E R O F F I C E M E M O R A N D U M

Date: 26-Oct-1992 08:48am EST
From: Robert Pollock
POLLOCK
Dept: HFD-230
Tel No: 301-295-8315

Margo Bennett (BENNETT)
Cecelia Parise (PARISEC)
Willie Turner (TURNERW)
William Rickman (RICKMAN)
Gordon Johnston (JOHNSTON)
J. Doleski (DOLESKI)
Harvey Greenberg (GREENBERG)
Ted M. Sherwood (SHERWOODT)

Roger Williams (WILLIAMSR)
Kent T. Johnson HFD-631 (GENERIC DR (JOHNSON)

ct: Tpoical corticosteroids

elow:

The interim guidance on topical corticosteroids issued on July 1, 1992. tudy initiated (first dosed) after that date should generally conform to ecommendations of the guidance. The guidance identifies three methdos of ating the performance of topical corticosteriods:

1. Pharmacodynamic Studies - the vasoconstricor assay

2. Dermatopharmacokinetic Studies - skin stripping studies

3. In-Vitro Release Studies - Franz cell studies

a regulatory standpoint #1 is a requirement, and #2 and #3 are not required condition of approval. The information gained from methods #2, and #3 may eful one day in establishing batch to batch release specification and may ually even provide sufficient data to support some type of in-vivo/in-vitro lation.

illiams will be requesting that all submissions contain a vasoconstrictor (required) and In-Vitro release studies (not mandated but information OGD like to see). From this perspective, PSS staff will screen all topical costeroids for this data. If no vasoconstrictor assay accompanies the ssion, the application will not be filed. Failure to include in-vitro se data will not be reason to refuse to file an application.

ır pect to receive submissions for topical corticosteroids that will .. ıdies initiated prior to July 1, 1992 and those that contain studies ıted after July 1, 1992 conducted under the new methodology outlined in ıterim Guidance. Dr. Williams would like the Division of Bioequivalence to the "new" studies but would like the Division of Anti-Infective drugs to

nu -o review vasoconstrictor assays conducted under the "old" methodology
cally 1 point measurements).

is E-mail, please initiate the change suggested above. That is:

1. Evaluate the studies submitted in all incoming applications for
al corticosteroids to determine the initiation date.

2. For all studies initiated (first dosed) after 7/1/92 be certain the
design conplies with the "new" Interim Guidance.

3. If the study was initiated after 7/1/92 and it was not conducted in
d with the "new" Interim Guidance, prepare a RF letter to the firm.

4. If the study complies with the "new" Interim Guidance it should be
red to the DIVISION OF BIOEQUIVALENCE for their review.

5. If the study was initiated prior to 7/1/92, consult the study for
w to the DIVISION OF ANTI-INFECTIVE DRUG PRODUCTS, HFD-520, as in the past.

certain there are no inconsistencies in these practices please review all
cations for topical corticosteroids submitted since 7/1/92 to determine if
ecisions to accept for filing and where to consult the study have been made
cord with the above guidance.

ring the initial review of any topical corticosteroid application, there is
stion of the appropriate course of action to be taken, see Gordon or myself
larification.

s,

ollock