CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 50-741

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: NDA 50741/000
Stamp: 14-MAY-1996 Regulatory Due: 06-SEP-2000
Applicant: STIEFEL LABS
255 ALHAMBRA CIR STE 1000
CORAL GABLES, FL 33134

Priority: 4S Org Code: 540
Action Goal: District Goal:
Brand Name: CLINDOXYL GEL(CLINDAMYCIN PHOSPHATE/BENZ
Established Name:
Generic Name: CLINDAMYCIN PHOSPHATE/BENZOYL PEROXIDE
Dosage Form: GEL (GEL)
Strength: 1% CLINDAMYCIN, 5% BEN

FDA Contacts:			
	O. CINTRON	(HFD-540)	301-827-2023 , Project Manager
	J. VIDRA	(HFD-540)	301-827-2065 , Review Chemist
	W. DECAMP II	(HFD-540)	301-827-2041 , Team Leader

Overall Recommendation:

ACCEPTABLE on 25-JUL-2000 by M. EGAS (HFD-322) 301-594-0095
WITHHOLD on 18-DEC-1996 by M. EGAS (HFD-322) 301-594-0095

Establishment:

DMF No:
AADA No:

Profile: CFN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 04-APR-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities:

Establishment:

DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-JUL-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities:

Establishment: 1314819
STIEFEL LABORATORIES INC
RT 145
OAK HILL, NY 12460

DMF No:
AADA No:

Profile: OIN OAI Status: NONE

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Responsibilities: FINISHED DOSAGE MANUFACTURER

Last Milestone: OC RECOMMENDATION
Milestone Date: 12-APR-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: 1316245
STIEFEL RESEARCH INSTITUTE INC
RT 145
OAK HILL, NY 14260

DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 04-APR-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE STABILITY TESTER

APPEARS THIS WAY
ON ORIGINAL

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 50741/000**
Priority: **4S** Org Code: **540**
Stamp: **14-MAY-1996** Regulatory Due: **26-AUG-2002**
Action Goal: District Goal:
Applicant: **STIEFEL LABS**
255 ALHAMBRA CIR STE 1000
CORAL GABLES, FL 33134
Brand Name: **CLINDOXYL GEL(CLINDAMYCIN PHOSPHATE/BENZ**
Established Name:
Generic Name: **CLINDAMYCIN PHOSPHATE/BENZOYL PEROXIDE**
Dosage Form: **GEL (GEL)**
Strength: **1% CLINDAMYCIN, 5% BEN**

FDA Contacts:

V. LUTWAK	**(HFD-540)**	**301-827-2020**	**, Project Manager**
J. VIDRA	**(HFD-540)**	**301-827-2065**	**, Review Chemist**
W. DECAMP II	**(HFD-540)**	**301-827-2041**	**, Team Leader**

Overall Recommendation:

ACCEPTABLE on 19-AUG-2002 by J. D AMBROGIO (HFD-324) 301-827-0062
ACCEPTABLE on 25-JUL-2000 by EGASM
WITHHOLD on 18-DEC-1996 by EGASM

Establishment:
DMF No:
AADA No:

Profile: **CFN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **05-AUG-2002**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities:

Establishment:
DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **19-AUG-2002**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities:

Establishment:
DMF No:
AADA No:

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **25-JUL-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: **1314819**
STIEFEL LABORATORIES INC
RT 145
OAK HILL, NY 12460

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **14-MAR-2002**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**
FINISHED DOSAGE STABILITY TESTER

Profile: **OIN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **15-MAR-2002**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

APPEARS THIS WAY
ON ORIGINAL

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: NDA 50741/000
Stamp: 14-MAY-1996 Regulatory Due: 06-SEP-2000
Applicant: STIEFEL LABS
255 ALHAMBRA CIR STE 1000
CORAL GABLES, FL 33134

Priority: 4S Org Code: 540
Action Goal: District Goal:
Brand Name: CLINDOXYL GEL(CLINDAMYCIN PHOSPHATE/BENZ
Established Name:
Generic Name: CLINDAMYCIN PHOSPHATE/BENZOYL PEROXIDE
Dosage Form: GEL (GEL)
Strength: 1% CLINDAMYCIN, 5% BEN

FDA Contacts:

O. CINTRON	(HFD-540)	301-827-2023	, Project Manager
J. VIDRA	(HFD-540)	301-827-2065	, Review Chemist
W. DECAMP II	(HFD-540)	301-827-2041	, Team Leader

Overall Recommendation:

ACCEPTABLE on 25-JUL-2000 by M. EGAS (HFD-322) 301-594-0095
WITHHOLD on 18-DEC-1996 by M. EGAS (HFD-322) 301-594-0095

Establishment:
DMF No:
AADA No:

Profile: CFN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 04-APR-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
Responsibilities: I

Establishment:
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 25-JUL-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
Responsibilities:

Establishment: 1314819
STIEFEL LABORATORIES INC
RT 145
OAK HILL, NY 12460
DMF No:
AADA No:

Profile: OIN OAI Status: NONE

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Last Milestone: **OC RECOMMENDATION**
Milestone Date: **12-APR-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Establishment: **1316245**
STIEFEL RESEARCH INSTITUTE INC
RT 145
OAK HILL, NY 14260

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **04-APR-2000**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **FINISHED DOSAGE STABILITY TESTER**

APPEARS THIS WAY
ON ORIGINAL

CDER Establishment Evaluation Report
for March 25, 1997

Application: NDA 50741/000
Stamp: 14-MAY-1996 Regulatory Due: 14-MAY-1997
Applicant: STIEFEL LABS
255 ALHAMBRA CIR STE 1000
CORAL GABLES, FL 33134

Priority: 4S Org Code: 540
Action Goal: District Goal:
Brand Name: CLINDOXYL GEL(CLINDAMYCIN P
Established Name:
Generic Name: CLINDAMYCIN PHOSPHATE/BENZ(
Dosage Form: BLK (BULK)
Strength:

FDA Contacts: N. MOKHTARI REJALI (HFD-540) 301-827-2065 , Review Chemist
W. DECAMP II (HFD-540) 301-827-2041 , Team Leader

Overall Recommendation:

WITHHOLD on 18-DEC-1996 by M. EGAS (HFD-324) 301-827-0062

Establishment:
DMF No:

Profile: CSN OAI Status: OAI ALERT
Last Milestone: OC RECOMMENDATI 05-NOV-1996
Responsibilities:
Decision: WITHHOLD
Reason: APPLICATION INTEGRITY POLICY

Establishment:
DMF No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATI 05-NOV-1996
Responsibilities:
Decision: ACCEPTABLE
Reason: BASED ON FILE REVIEW

Establishment: 1314819
STIEFEL LABORATORIES INC
RT 145
OAK HILL, NY 12460
DMF No:

Profile: OIN OAI Status: NONE
Last Milestone: OC RECOMMENDATI 05-NOV-1996
Responsibilities:
FINISHED DOSAGE MANUFACTURER
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

K1.2A

NDA 50-741
Response to NA Letter 9/6/

N50741

REC 9/4/02 9:25AM

DUAC Topical Gel
(clindamycin, 1% - benzoyl peroxide, 5%)

Indication: DUAC Topical Gel is indicated for the topical treatment of inflammatory acne vulgaris

Sponsor: Stiefel laboratories, Inc.

Submitted: February 22, 2002
Stamp Date: February 26, 2002
PDUFA Due Date: August 26, 2002)

Reviewers
Clinical: Phyllis Huene
Chemistry: Jim Vidra
Pharmacology: Paul Brown
Biopharmacology:
Statistician: Kathleen Fritsch
Microbiology: Harold Silver

Team Leaders
Clinical: Markham C. Luke
Chemistry: Tony DeCamp
Pharmacology: Abby Jacobs
Biopharmacology: Dennis Bashaw
Statistician: Mohamed Alosh
Project Manager
Victoria Lutwak

Vol. 2

NDA 50-741
Response to NA Letter 9/6/00

INDs

Clindoxyl
(clindamycin phoshate / benzoyl peroxide)
Gel
Indication: For the treatment of inflammatory lesions of acne vulgaris, only

Sponsor: Stiefel laboratories, Inc.

Submitted: February 22, 2002
Stamp Date: February 26, 2002
PDUFA Due Date: August 26, 2002 (Monday)

Reviewers
Clinical: Phyllis Huene
Chemistry: Jim Vidra
Pharmacology: Paul Brown
Biopharmacology:
Statistician: Kathleen Fritsch
Microbiology: Paul Stinavage

Team Leaders
Clinical: Susan Walker
Chemistry: Tony DeCamp
Pharmacology: Abby Jacobs
Biopharmacology: Dennis Bashaw
Statistician: Mohamed Alosh
Project Manager
Victoria Lutwak

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-239-6341

12 June 1996

Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: **NDA 50-741**
Clindoxyl™ Gel
(clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide)

Dear Sir/Madam:

This letter will serve to confirm that all clinical data and all safety data has been submitted for Study #150, Study # 151, and Study #152. The data was included in the original New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Please note that the "completed" status of subject studies was previously reported in the Integrated Summary of Safety Information, Item 8.H., Volume 1.16, page 221 of NDA 50-741.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President
Regulatory Affairs and
Quality Assurance

WAC:mjt

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-239-6341

March 15, 2002

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., HFD-540
2nd Floor North
Rockville, MD 20850

RE: **TELEPHONE AMENDMENT**
NDA 50-741
Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Dear Sir/Madam:

We here confirm all available safety information has been submitted to the U.S. Food and Drug Administration specific to Clindoxyl™ Topical Gel (clindamycin – benzoyl peroxide), NDA 50-741.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjc

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-239-6341

March 15, 2002

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., HFD-540
2nd Floor North
Rockville, MD 20850

RE: **TELEPHONE AMENDMENT**
NDA 50-741
Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Dear Sir/Madam:

We here confirm that on December 11, 2000 Stiefel Canada Inc., Montreal, Quebec Canada (Stiefel Laboratories International Division) received a Notice of Compliance from Health Canada, Therapeutic Products Directorate for Clindoxyl Gel (DIN 02243158).

Clindoxyl Gel was introduced to the Canadian market on September 4, 2001. To date a total of _____ have been distributed. There have been a total of nine (9) complaints of skin irritation associated with Clindoxyl Topical Gel as of March 15, 2002.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjc

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-239-6341

March 15, 2002

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., HFD-540
2nd Floor North
Rockville, MD 20850

RE: **TELEPHONE AMENDMENT**
NDA 50-741
Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Dear Sir/Madam:

We here confirm that on July 16, 1999 Stiefel Mexicana S.A de C.V. recieved approval for Clindoxyl Topical Gel under the tradename INDOXYL (registration #320M99SSA).

The product has not been introduced into commercial distribution, therefore, there have been no reports of drug product adverse reactions.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjc

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-239-6341

March 15, 2002

Division of Dermatologic and Dental Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Blvd., HFD-540
2nd Floor North
Rockville, MD 20850

RE: **TELEPHONE AMENDMENT**
NDA 50-741
Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Dear Sir/Madam:

We here confirm drug substance(s), benzoyl peroxide, USP and clindamycin phosphate, USP, [redacted]™ Topical Gel (clindamycin – benzoyl peroxide) are manufactured at the following locations:

Benzoyl Peroxide, USP:

Tradename:

Manufacturing Address: [redacted]

[redacted]

Central File Number:

Mailing Address: [redacted]

Corporate Headquarters: [redacted]

Clindamycin Phosphate, USP:

Manufacturing Address: [redacted]

Central File Number:

Corporate Headquarters: [redacted]

We also here confirm drug product, Clindoxyl Topical Gel (clindamycin-benzoyl peroxide), is manufactured at:

Manufacturing Address:	Stiefel Laboratories, Inc. Route 145 Oak Hill, New York 12460
Central File Number:	1314819
Corporate Headquarters:	Stiefel Laboratories, Inc. 255 Alhambra Circle, Suite 1000 Coral Gables, Fl 33134

We here confirm that all sites referenced above are, and will remain, ready for inspection by FDA.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjc

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Stiefel Laboratories, Inc.	March 15, 2002
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
(305) 443-3800	(305) 443-3467
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code telephone & FAX number)* IF APPLICABLE
255 Alhambra Circle, Suite 1000 Coral Gables, FL 33134	Not Applicable

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) NDA 50-741

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clindamycin Phosphate and Benzoyl Peroxide	Clindoxyl™ Gel

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)* Methyl 7-chloro-6,7,8-trideoxy-6-(l-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate) and benzoyl peroxide

CODE NAME *(If any)* Not Applicable

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Gel	Clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide	Topical

(PROPOSED) INDICATION(S) FOR USE: Acne vulgaris

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 31.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Not Applicable Holder of Approved Application Not Applicable

TYPE OF SUBMISSION *(check one)*
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION Response to FDA's 14 March 2002 telephone request for electronic labeling (pdf.)

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See attached.

ess References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current plication)

See attached.

This application contains the following items: *(Check all that apply)*	
	1. Index
XX	2. Labeling *(check one)* ☒ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50(c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50(d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355 (b) (2) or (j) (2) (A)
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k) (1))
	17. Field copy certification (21 CFR 314.50(k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	William A. Carr, Jr. Vice President	3/15/2002

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
Route 145 Oak Hill New York 12460	(518) 239-6901

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

DRUG SUBSTANCE(S):

CLINDAMYCIN PHOSPHATE:

MANUFACTURER(S):

NAME:

ADDRESS:

TELEPHONE:
FACSIMILE:

CONTACT:

CLINDAMYCIN PHOSPHATE:

MANUFACTURER(S):

NAME:

ADDRESS:

TELEPHONE:
FACSIMILE:

CONTACT:

BENZOYL PEROXIDE:
MANUFACTURER(S):

NAME:

Mfg Address:

Mailing Address:

TELEPHONE:
FACSIMILE:

CONTACT:

DRUG PRODUCT: Clindoxyl™ Gel
(clindamycin phosphate equivalent to
1% clindamycin and 5% benzoyl peroxide)

NDA 50-741

MANUFACTURER:

NAME: Stiefel Laboratories, Inc.

ADDRESS: Corporate Headquarters:
255 Alhambra Circle, Suite 1000
Coral Gables, FL 33134

TELEPHONE: 305-443-3800
FACSIMILE: 305-443-3467

MANUFACTURING: Route 145
Oak Hill, NY 12460

TESTING/STABILITY: Route 145
Oak Hill, New York 12460

*Testing/Stability testing is performed by A.C. Stiefel Research Institute, Inc. – a wholly owned subsidiary o f Stiefel Laboratories, Inc.

CONTACT: William A. Carr, Jr.
Vice President

TELEPHONE: 518-239-6901
FACSIMILE: 518-239-8402

CENTRAL FILE NUMBER(S):
Stiefel Laboratories, Inc.: 1314819
A.C. Stiefel Research Institute, Inc.: 1316245

We here confirm that all sites referenced above are, and will remain, ready for inspection by FDA.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

Drug Substance:

Clindamycin Phosphate:

Contatiner/Closure System:

APPEARS THIS WAY
ON ORIGINAL

K1.1A

K1.1A

N50741

N50741

NDA 50-741

Response to NA Letter 9/6/00

REC.
9/4/02
9:25AM

IND

DUAC Topical Gel

(clindamycin, 1% - benzoyl peroxide, 5%)

Indication: DUAC Topical Gel is indicated for the topical treatment of inflammatory acne vulgaris

Sponsor: Stiefel laboratories, Inc.

Submitted: February 22, 2002
Stamp Date: February 26, 2002
PDUFA Due Date: August 26, 2002)

Reviewers
Clinical: Phyllis Huene
Chemistry: Jim Vidra
Pharmacology: Paul Brown
Biopharmacology:
Statistician: Kathleen Fritsch
Microbiology: Harold Silver

Team Leaders
Clinical: Markham C. Luke
Chemistry: Tony DeCamp
Pharmacology: Abby Jacobs
Biopharmacology: Dennis Bashaw
Statistician: Mohamed Alosh
Project Manager
Victoria Lutwak

Vol. 1

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 50-741	Efficacy Supplement Type SE-	Supplement Number	
Drug: DUAC (clindamycin, 1% - benzoyl peroxide, 5%) Topical Gel.		Applicant: Stiefel Laboratories, Inc	
RPM: V. Lutwak		HFD-540	Phone # 301-827-2073
Application Type: (x) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(x) Standard ( ) Priority
• Chem class (NDAs only)	4S Anti-bacterial agent
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	August 26, 2002
❖ Special programs (indicate all that apply)	(x) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(x) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (x) No
• This application is on the AIP	( ) Yes ( ) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(x) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(x) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	Only for an approval x
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ ( ) No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	
General Information	
❖ Actions	
• Proposed action	(x) AP ( ) TA (x) AE ( ) NA
• Previous actions (specify type and date for each action taken)	05/14/97, NA , 01/30/98, NA, and 09/06/02, NA
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (x) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(x) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	x
• Most recent applicant-proposed labeling	x
• Original applicant-proposed labeling	x
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	e-mail 8-14-02 labeling day July 1, 2002
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	X BenzaClin
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	x
• Applicant proposed	x
• Reviews	x
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	Yes t-con see 08/20/02
• Documentation of discussions and/or agreements relating to post-marketing commitments	See fax 08/20/02
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Yes.
❖ Memoranda and Telecons	Yes.
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	none
• Pre-NDA meeting (indicate date)	none
• Pre-Approval Safety Conference (indicate date; approvals only)	NA
• Other	Dispute Resolution

❖ Advisory Committee Meeting	
• Date of Meeting	NA
• 48-hour alert	
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	August 15, 2002; August 15, 2000; May 13, 1994
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	August 5, 2002; November 17, 00
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	See tab-
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	See tab- reviewer's comment and peds waiver
❖ Statistical review(s) *(indicate date for each review)*	June 25, 2002; July 17, 2000; Feb. 10, 1997
❖ Biopharmaceutical review(s) *(indicate date for each review)*	Sept 1, 2000, labeling review 8-02
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	NA 8/14/02
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	NA
• Bioequivalence studies	NA
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	August 21, 2002
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	NA
• Review & FONSI *(indicate date of review)*	
• Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	NA
❖ Facilities inspection (provide EER report)	Date completed: 08/19/02 (x) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed NA ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	08/04/02
❖ Nonclinical inspection review summary	NA
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	Phase 4 commitment
❖ CAC/ECAC report	Phase 4 commitment

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 50-741 /SE____ - _____

Drug Clindoxyl Gel Applicant Stiefel Laboratories

RPM O. Cintron Phone 7-2020

☑ 505(b)(1)
☐ 505(b)(2) Reference listed drug _____

☐ Fast Track ☐ Rolling Review Review priority: ☑ S ☐ P

Pivotal IND(s) _____

Application classifications:
Chem Class 45
Other (e.g., orphan, OTC) —

PDUFA Goal Dates:
Primary —
Secondary SEPT 6 00

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: ☑ User Fee Paid
  ☐ User Fee Waiver (attach waiver notification letter)
  ☐ User Fee Exemption

- Action Letter..... ☐ AP ☐ AE ☑ NA

- Labeling & Labels
  FDA revised labeling and reviews..... (deferred) N/A (not approvable)
  Original proposed labeling (package insert, patient package insert) ..... included
  Other labeling in class (most recent 3) or class labeling..... —
  Has DDMAC reviewed the labeling? ..... ☐ Yes (include review) ☑ No
  Immediate container and carton labels ..... included (proposed)
  Nomenclature review ..... included (COPRA)

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is ☑ is not on the AIP.
  Exception for review (Center Director's memo)..... —
  OC Clearance for approval..... EER included

Continued ⇨

- Safety Update review(s) ..... included in NO review.

- Pediatric Information
  ☑ Waiver/partial waiver (Indicate location of rationale for waiver) ☐ Deferred
  Pediatric Page..... in M.O. review
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☐ Not Applicable NO

- Statistical review(s) and memoranda 7/17/00

- Biopharmaceutical review(s) and memoranda..... 9/1/2000

- Abuse Liability review(s) ..... N/A
  Recommendation for scheduling ..... N/A

- Microbiology (efficacy) review(s) and memoranda ..... APRIL 13/00

- DSI Audits ..... e-mail included
  ☑ Clinical studies ☐ bioequivalence studies .....

CMC INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- CMC review(s) and memoranda 8/23/00

- Statistics review(s) and memoranda regarding dissolution and/or stability ..... N/A

- DMF review(s) ..... NO

- Environmental Assessment review/FONSI/Categorical exemption ..... N/A

- Micro (validation of sterilization) review(s) and memoranda ..... N/A

- Facilities Inspection (include EES report)
  Date completed JULY/25/00 ..... ☑ Acceptable ☐ Not Acceptable

- Methods Validation ..... ☐ Completed ☑ Not Completed

PRECLINICAL PHARM/TOX INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- Pharm/Tox review(s) and memoranda 8/22/00

- Memo from DSI regarding GLP inspection (if any) ..... e-mail none

Continued ⇨

- Statistical review(s) of carcinogenicity studies ..... no carc. studies
- CAC/ECAC report ..... N/A

APPEARS THIS WAY
ON ORIGINAL

OFFICES OF DRUG EVALUATION
ORIGINAL NDA/NDA EFFICACY SUPPLEMENT
ACTION PACKAGE CHECKLIST

NDA #__50-741_____ Drug: Clindoxyl (clindamycin/benzoyl peroxide) Gel _____

Applicant:_Stiefel Laboratories_____ Chem/Ther/other Types:____4S_____

CSO/PM:_White_____ Phone:_7-2072_____ HFD-_540_____

USER FEE GOAL DATE:___May 14, 1997___ DATE CHECKLIST COMPLETED:_5/13/97_____

Arrange package in the following order (include a completed copy of this CHECKLIST): Check or Comment

1. ACTION LETTER with supervisory signatures — AP_____ AE_____ NA__✓____
   Are there any Phase 4 commitments? — Yes_____ No_____
2. Have all disciplines completed their reviews? — Yes_____ No_____
   If no, what review(s) is/are still in draft?
   _____
3. LABELING (package insert and carton and container labels). — Draft__deferred__
   (If final or revised draft, include copy of previous version with ODE's comments and state where in action package the Division's review is located. If Rx-to-OTC switch, include current Rx Package insert and HFD-312 and HFD-560 reviews of OTC labeling.) — Revised Draft_____ Final_____
4. PATENT INFORMATION — _____✓_____
5. EXCLUSIVITY CHECKLIST — __deferred__
6. PEDIATRIC PAGE (all NDAs) — _____✓_____
7. DEBARMENT CERTIFICATION
   (Copy of applicant's certification for all NDAs submitted on or after June 1, 1992). — _____✓_____
8. Statement on status of DSI's AUDIT OF PIVOTAL CLINICAL STUDIES — _____✓_____
   If AE or AP ltr, explain if not satisfactorily completed. Attach a COMIS printout of DSI status.
   If no audits were requested, include a memo expaining why.
9. REVIEWS & MEMORANDA:

DIVISION DIRECTOR'S MEMO	If more than 1 review for any	_____
GROUP LEADER'S MEMO	1 discipline, separate reviews	_____
MEDICAL REVIEW	with a sheet of colored paper.	_____3/4/97_____
SAFETY UPDATE REVIEW	Any conflicts between reviews	_____n/a_____
STATISTICAL REVIEW	must have resolution documented	___2/10/97;_5/12/97__
BIOPHARMACEUTICS REVIEW		_____5/12/97_____
PHARMACOLOGY REVIEW (Include pertinent IND reviews)		_____10/31/97____
Statistical Review of Carcinogenicity Study(ies)		_____n/a_____
CAC Report/Minutes		_____n/a_____
CHEMISTRY REVIEW		_____5/9/97_____
Labeling and Nomenclature Committee Review Memorandum (send 4/10/97)		_____
Date EER completed _3/26/97_ (attach signed form or CIRTS printout)		OK_____ No__✓____
FUR needed _____ FUR requested		
Have the methods been validated?		Yes (attach)___✓____ No_____
Environmental Assessment Review / FONSI		Review _deferred_ FONSI_____
MICROBIOLOGY REVIEW		_____11/7/96_____
What is the status of the monograph?		_____n/a_____

10. CORRESPONDENCE, MEMORANDA OF TELECONS, and FAXes — _____✓_____
11. MINUTES OF MEETINGS — _____n/a_____
    Date of End-of-Phase 2 Meeting: _____
    Date of pre-NDA Meeting: _____
12. ADVISORY COMMITTEE MEETING MINUTES — Minutes_____ Info Alert_____
    or, if not available, 48-Hour Info Alert or pertinent section of transcript. — Transcript_____ No mtg___✓__
13. FEDERAL REGISTER NOTICES; OTC or DESI DOCUMENTS — _____n/a_____
14. If approval letter, has ADVERTISING MATERIAL been reviewed? — Yes_____ No_____
    If no and this is an AP with draft labeling letter, has advertising material already been requested? — Yes, documentation attached_____ No, included in AP ltr _____

15. INTEGRATED SUMMARY OF EFFECTIVENESS (from NDA) _____✓_____

16. INTEGRATED SUMMARY OF SAFETY (from NDA) _____✓_____

revision: 5/14/96;edited LR:5/28/96

APPEARS THIS WAY
ON ORIGINAL

NDA 50-741

CLINDOXYL GEL

(clindamycin phosphate/benzoyl peroxide)

Stiefel Laboratories, Inc.

TYPE "4S"

USER FEE GOAL DATE: 5/14/97

(VOLUME 1 OF 1)

REVIEW TEAM:

1. MEDICAL OFFICER	S. WALKER
2. PHARM/TOX	K. MAINIGI
3. CHEMISTRY	N. MOKHTARI-REJALI
4. MICROBIOLOGY	P. STINAVAGE
5. BIOPHARMACEUTICS	D. BASHAW
6. BIOSTATISTICS	V. FREIDLIN
7. PROJECT MANAGER	K.D. WHITE (X7-2020)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 50-741

SEP 6 2000

Siefel Laboratories, Inc.
Attention: Mr. William A. Carr, Jr.
Route 145
Oak Hill, NY 12460

Dear Mr. Carr:

Please refer to your new drug application (NDA) dated May 3, 1996, received May 14, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clindoxyl (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) Gel.

We acknowledge receipt of your submissions dated April 4 and 13, May 1 and 2, June 20 and 29, July 14 (two), and August 8, 2000. Your submission of March 3, 2000, constituted a complete response to our May 14, 1997, and January 30, 1998, action letters.

We have completed our review and find the information presented is inadequate, and the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

A. Chemistry:

1. There is an absence of comparative data that indicate equivalence between the —— and ——. clindamycin phosphates. These data should include comparisons of: chemical/physical properties, specifications, impurity profiles and stability data for both drug substances and when each is formulated into Clindoxyl Gel.

2. A minimum 12 months stability data of the Clindoxyl Gel formulated with the —— clindamycin phosphate and aged in the commercial package was not submitted. The ICH-Q1A on Stability Guideline should be followed for the recommended batch sizes on three individual stability batches.

B. Clinical:

The clinical studies submitted (Studies 156 and 158) did not demonstrate that Clindoxyl Gel is superior in effectiveness to the benzoyl peroxide gel alone. We recommend an adequate and well-controlled, additional clinical trial evaluating the safety and efficacy of Clindoxyl Gel versus benzoyl peroxide gel in the treatment of acne vulgaris. Such a study would have to demonstrate clinical superiority of the Clindoxyl Gel over the benzoyl peroxide gel alone.

Although not the basis for the Not Approvable action for this application, the following issues should be addressed in the resubmission:

A. Chemistry:

1. Please submit the justification for the hydrous benzoyl peroxide related substance, specifications since none is included in the USP monograph for this bulk drug.

2. Please provide a post-approval commitment statement to determine the viscosity at release and at each stability time point for the first five production batches.

Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you update your NDA by submitting all safety information you now have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.

2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.

3. Details of any significant changes or findings.

4. Summary of worldwide experience on the safety of this drug.

5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

6. English translations of any approved foreign labeling not previously submitted.

7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with this division to discuss what further steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Olga I. Cintron, R.Ph., Project Manager, at (301) 827-2020.

Sincerely,

/S/

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental
Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

NDA 50-741

JAN 30 1998

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Route 145, Oak Hill, NY 12460

Dear Mr. Carr:

Please refer to your new drug application dated May 3, 1996, received May 14, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clindoxyl (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) Gel.

Please refer to your not approvable letter dated May 14, 1997.

We have completed our review of the acceptability of clinical studies conducted with clindamyacin phosphate, USP, manufactured by ——— , currently under the Agency's "Application Integrity Policy" (AIP) (56 Federal Register 46191) and find the quality of the data inadequate to support the aforementioned NDA application. In addition, because of the uncertain quality of the AIP materials, clinical studies conducted using this bulk drug can not be used to support drug product claims either directly or indirectly.

This application is therefore not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The not approvable issue identified in this letter supersedes the deficiencies noted in our not approvable letter dated May 14, 1997.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendments should respond to all the deficiencies listed in this letter. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

If you have any questions, please contact Mr. Kevin Darryl White, M.B.A., Regulatory Health Project Manager, at (301) 827-2020.

Sincerely yours,

/S/

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 50-741
HFD-540/Div. files
HFD-002/ORM
HFD-105/Weintraub
HFD-101/L.Carter
HFD-830/Sheinin
DO-BUF
HFD-92/DDM-DIAB
HFD-540/DIV DIR/Wilkin
HFD-540/ACTG DERM TL/Walker
HFD-540/MO/Toombs
HFD-560/CHEM/Mokhtari-Rejali
HFD-540/CHEM TL/DeCamp
HFD-540/PHARM/Mainigi
HFD-540/PHARM TL/Jacobs
HFD-805/MICRO/Stinavage
HFD-805/MICRO TL/Cooney
HFD-725/BIOSTAT/Freidlin
HFD-725/BIOSTAT TL/Srinivasan
HFD-880/BIOPHARM/Bashaw
HFD-880/BIOPHARM/Lazor
HFD-540/SUPV PROJ MGR/Kozma-Fornaro
HFD-540/PROJ MGR/White

Drafted by: KDW/November 21, 1997
Initialed by:
final:

NOT APPROVABLE (NA)

APPEARS THIS WAY
ON ORIGINAL

HFD 540/WH

NDA 50-741

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Route 145, Oak Hill, NY 12460

MAY 14 1997

Dear Mr. Carr:

Please refer to your new drug application dated May 3, 1996, received May 14, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Clindoxyl (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) Gel.

We acknowledge receipt of your submissions dated June 12 (two), 14, 19, and 24 (four), August 1 and 27, and September 27 (two), 1996; January 31, and May 5 (three), 1997. The User Fee goal date for this application is May 14, 1997.

We have completed our review and find the information presented is inadequate, and the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies are summarized as follows:

A. Chemistry

1. The referenced —— , supplier of clindamycin phosphate, has been withdrawn by —— A new supplier should be identified.

2. The regulatory specifications should include limits for all known degradation products of clindamycin in the presence of benzoyl peroxide in the gel formulation. In addition, please include the spectra for all principle degradation products in Clindoxyl Gel.

3. The stability data do not support the high limits for related compounds. Please provide justification for related substances specification in Clindoxyl Gel.

4. Please submit the chemical degradation pathway for impurities of Clindoxyl Gel.

B. Clinical

1. The efficacy of Clindoxyl Gel has not been demonstrated over benzoyl peroxide gel alone in the treatment of lesions of acne vulgaris. We recommend an additional clinical trial investigating the safety and efficacy of Clindoxyl Gel versus benzoyl peroxide gel in the treatment of acne vulgaris, in order to establish the clinical superiority of Clindoxyl Gel over benzoyl peroxide gel alone.

Although not the basis for the Not Approvable action of this application, the following areas should be addressed in any resubmission:

A. Chemistry

1. Please submit the justification for benzoyl peroxide related substances' specifications, since these are not included in the USP monograph.

2. The flow chart of manufacturing process of bulk Clindoxyl Gel should be submitted.

3. Please provide a post-approval commitment statement to determine the viscosity for the first five batches. Based on these measurements, a viscosity specification should be proposed as a release specification as well as stability specification.

4. Stability data should be submitted for all batches manufactured from the new supplier to support the two years expiry date. These data should be compared to the stability data presented in the original clinical trials.

5. An updated Environmental Assessment package, including a revision of your non-confidential statement information of August 27, 1996, should be resubmitted when a new supplier for clindamycin phosphate is identified.

B. Clinical

1. Failure to demonstrate that Clindoxyl Gel poses a minimal safety hazard to patients as a contact sensitizer.

C. Biopharmaceutics

1. There is no assessment of the degree or relative nature of the in vivo percutaneous absorption of clindamycin and benzoyl peroxide from Clindoxyl Gel. Prior to resubmission, please provide an in vitro assessment of the percutaneous absorption of both clindamycin and benzoyl peroxide from Clindoxyl Gel, Cleocin-T® Solution, and a single entity product of benzoyl peroxide. Provided that these in vitro studies show that the rate and/or extent of in vitro percutaneous penetration is less than that of Cleocin-T® or the single entity benzoyl peroxide product, then in vivo bioavailability testing will not be required. If such studies show enhanced percutaneous penetration for the Clindoxyl Gel dosage form, then an assessment of the in vivo percutaneous absorption of Clindoxyl Gel in man will be required. Please submit all proposed protocols to the Agency for review and comment before study initiation.

D. Microbiology

1. Please be aware that it is not possible to define the term "any other etiologic agent." The term, as written in the drug product specification, encompasses a very large number of microorganisms. As written, it would not be possible to meet these criteria. OK

2. Antimicrobial preservative effectiveness testing should be performed on the first three production lots of product as part of the stability protocol. At a minimum, this testing should be performed initially and at product expiry. Please provide a commitment to perform this testing. OK

E. Pharmacology/Toxicology

1. The issue of potential carcinogenicity and/or photocarcinogenicity of benzoyl peroxide has not been resolved. Therefore, as with all other benzoyl peroxide products, the label should contain the required warning about exposure to sun and incorporate revisions after ongoing NMDA studies have been reviewed. Phase 4 studies may be needed, if Clindoxyl Gel is not photostable under conditions of use. OK

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendments should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

If you have any questions, please contact Mr. Kevin Darryl White, M.B.A., Regulatory Health Project Manager, at (301) 827-2020.

Sincerely yours,

/S/

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 50-741
HFD-540/Div. files
HFD-002/ORM
HFD-105/Weintraub
HFD-101/L.Carter
HFD-830/Sheinin
DO-BUF
HFD-92/DDM-DIAB
HFD-540/DIV DIR/Wilkin
HFD-540/MO/Walker/SW 5.14.97
HFD-540/ACTG DERM TL/Toombs
HFD-560/CHEM/Mokhtari-Rejali/NMR 5.13.97
HFD-540/CHEM TL/DeCamp/WD 5.13.97
HFD-540/PHARM/Mainigi/KDM 5.13.97
HFD-540/PHARM TL/Jacobs/AJ 5.14.97
HFD-805/MICRO/Stinavage
HFD-805/MICRO TL/Cooney
HFD-725/BIOSTAT/Freidlin/VF 5.13.97
HFD-725/BIOSTAT TL/Srinivasan/RS 5.13.97
HFD-880/BIOPHARM/Bashaw/EDB 5.12.97
HFD-880/BIOPHARM/Lazor
HFD-540/SUPV PROJ MGR/Kozma-Fornaro/MJKF 5.13.97
HFD-540/PROJ MGR/White/KDW 5.12.97

Drafted by: /May 8, 1997/
Initialed by:
final:

NOT APPROVABLE (NA)

********** -COMM. JOURNAL- ********** DATE AUG-26-2002 ***** TIME 10:48 *********

MODE = MEMORY TRANSMISSION START=AUG-26 10:41 END=AUG-26 10:48

FILE NO.=677

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/EMAIL ADDRESS/TELEPHONE NO.	PAGES	DURATION
001	OK	#	915182398402	014/014	00:05:46

-FDA/CDER/DDDDP/HFD540 -

********** -301 827 2075 - ***** - 301 827 2075- **********

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE 5

FACSIMILE TRANSMITTAL SHEET

DATE: August 26 ~~23~~, 2002

To: William Carr	**From:** Victoria Lutwak VL
Company: Stiefel Laboratories, Inc	Division of Dermatological and Dental Drug Products
Fax number: 518-239-8402	**Fax number:** 301-827-2075
Phone number: 518-239-6901	**Phone number:** 301-827-2073

Subject: AP letter with labeling

Total no. of pages including cover:

Comments: See attached

See following pages.

Document to be mailed: ☒ YES ☐ NO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE 5

FACSIMILE TRANSMITTAL SHEET

DATE: August ~~23~~ 26, 2002

To: William Carr	**From:** Victoria Lutwak VL
Company: Stiefel Laboratories, NY	Division of Dermatological and Dental Drug Products
Fax number: 518-239-8402	**Fax number:** 301-827-2075
Phone number: 518-239-6901	**Phone number:** 301-827-2073
Subject: A.P. letter with labeling	

Total no. of pages including cover:

Comments: See attached

See following pages.

Document to be mailed: NA ☐ YES ☐ NO

Number of Pages Redacted

❖❖❖

Draft Labeling
(not releasable)

44 pages

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 7/ 27/ 2000	DUE DATE: 8/ 6/ 2000	OPDRA CONSULT #: 00-0195

TO:

Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
(HFD-540)

THROUGH:

Olga Cintron
Project Manager
(HFD-540)

PRODUCT NAME: Clindoxyl Gel (Clindamycin 1% and Benzoyl Peroxide 5% Gel) **NDA #:** 50-741	**MANUFACTURER:** Stiefel Laboratories, Inc.

SAFETY EVALUATOR: Lauren Lee, Pharm.D.

OPDRA RECOMMENDATION:

OPDRA recommends the labeling revisions listed in this review. In addition, see OPDRA consult# 00-0123 for our previous labeling recommendations.

/S/ 7/31/2000

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

/S/ 7/31/00

Peter Honig, MD
Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B-03
Center for Drug Evaluation and Research

FOLLOW-UP LABELING REVIEW

DATE REVIEWED: July 28, 2000

NDA#: 50-741

NAME OF DRUG: Clindoxyl Gel (Clindamycin 1% and Benzoyl Peroxide 5% Gel)

NDA HOLDER: Stiefel Laboratories, Inc.

I. INTRODUCTION:

This OPDRA consult is in response to a request received on July 27, 2000, from the Division of Dermatologic and Dental Drug Products, to re-review the proposed container label and the carton labeling for possible interventions in minimizing medication errors.

Clindoxyl Gel container labels and carton labeling were previously reviewed by the Office of Post-Marketing and Drug Risk Assessment (OPDRA) on June 21, 2000 as part of the proprietary name review.

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

The container labels and carton labeling received on July 27, 2000 are colored drafts of the previously reviewed label/labeling and do not include revisions recommended by OPDRA in the original consult. Therefore, see **OPDRA consult# 00-0123** for label/labeling recommendations. In addition, we have the following comments:

A. CONTAINER LABEL

1. We recommend that the established name be printed in letters that are at least half as large as the letters comprising the proprietary name to be in accordance with 21 CFR 201.10 (g) (2).

2. The proposed container labels for **Clindoxyl Gel** and **Clobevate Gel** (ANDA #: 75-027/ S-002) are similar except for the background color and slight adjustment in the location of the two diagonal stripes. Clobevate Gel is also manufactured by **Stiefel Laboratories**. In order to prevent medication errors due to the similar labels of these two **topical** products, we recommend revising Clindoxyl Gel container labels so that it would appear distinctively different. (e.g. different design & colors, boxing, bolding etc.).

3. The strength of the product is not easily noticeable due to its small font size. We recommend increasing the prominence of the strength.

B. CARTON LABELING

1. On the top tuck flap, we recommend adding the ——— the proprietary name to be in accordance with 21 CFR 201.10 (g) (1).

2. On the Professional Sample carton, the phrase, "Available in 45 gram tubes," is confusing in that the carton contains 5 gram tubes. We recognize that Clindoxyl Gel is also available in 45 gram tubes, but it is misleading to place this phrase on the sample carton. We recommend deleting the phrase, "Available in 45 gram tubes."

3. See comments under CONTAINER LABEL.

III. RECOMMENDATIONS:

OPDRA recommends the above labeling revisions that might lead to the safer use of the product. In addition, see OPDRA consult# 00-0123 for our previous labeling recommendations.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Lauren Lee, Pharm.D. at 301-827-3243.

/S/ 7/28/00

Lauren Lee, Pharm.D.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/ 7/31/2000

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

APPEARS THIS WAY
ON ORIGINAL

CC:

NDA: 50-741
Office Files
HFD-540; DivFiles; Olga Cintron, Project Manager
HFD-540; Jonathan Wilkin, Division Director
HFD-440; Mary Dempsey, Project Manager, DDRE II, OPDRA (Electronic Only)
HFD-400; Sammie Beam, Project Manager, Medication Errors, OPDRA (Electronic Only)
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (Electronic Only)
HFD-002; Mac Lumpkin, Deputy Center Director for Review Management
(Electronic Only)

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 4/ 13/ 2000	DUE DATE: 6/ 15/ 2000	OPDRA CONSULT #: 00-0123

TO:

Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
(HFD-540)

THROUGH:

Olga Cintron
Project Manager
(HFD-540)

PRODUCT NAME:	**MANUFACTURER:**
Clindoxyl Gel (Clindamycin 1% and Benzoyl Peroxide 5% Gel) **NDA #:** 50-741	Stiefel Laboratories, Inc.

SAFETY EVALUATOR: Lauren Lee, Pharm.D.

OPDRA RECOMMENDATION:

OPDRA has no objections to the use of the proprietary name, Clindoxyl Gel. See the checked box below.

FOR NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW

This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRAREQUEST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW

OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

☒ FOR PRIORITY 6 MONTH REVIEWS

OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDA's from this date forward.

/S/ /S/ 6/21/00

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

Peter Honig, MD
Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B-03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE RECEIVED: April 13, 2000

NDA#: 50-741

NAME OF DRUG: Clindoxyl Gel (Clindamycin 1% and Benzoyl Peroxide Hydrous 5% Gel)

NDA HOLDER: Stiefel Laboratories, Inc.

I. INTRODUCTION:

This OPDRA consult is in response to a April 13, 2000 request by the Division of Dermatologic and Dental Drug Products, to review the proposed proprietary drug name, Clindoxyl Gel, regarding potential name confusion with other proprietary/generic drug names. The container label, the carton labeling, and the package insert were reviewed for possible interventions in minimizing medication errors.

PRODUCT INFORMATION
Clindoxyl is a topical gel containing clindamycin 1% and benzoyl peroxide hydrous 5% gel. Clindamycin is an antibiotic and benzoyl peroxide is an antibacterial and keratolytic agent. Clindoxyl Gel is indicated for the topical treatment of acne vulgaris. The usual dosage is one application in the evening or as directed by a physician to affected areas. Clindoxyl Gel is supplied in a 45 g tube.

II. RISK ASSESSMENT

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts[1,2,3] as well as several FDA databases[4] for existing drug names which sound-alike or look-alike Clindoxyl Gel to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. An expert panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted prescription analysis studies consisting of written prescription studies and a verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

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[1] MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Emergindex, Reprodisk, Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2000).
[2] American Drug Index, online version, Facts and Comparisons, St. Louis, MO.
[3] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[4] Drug Product Reference File [DPR], the Established Evaluation System [EES], the AMF Decision Support System [DSS], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.
[5] WWW location http://www.uspto.gov/tmdb/index.html.

A. EXPERT PANEL DISCUSSION

[The expert panel consists of members of OPDRA's medication error Safety Evaluator Staff and a representative from the Division of Drug Marketing, Advertising and Communications (DDMAC)].

1. The panel identified [redacted] to be similar to Clindoxyl. *(Although the [redacted] . Therefore, there is no safety risk associated with this name.)* Furthermore, the stem, "doxy", implies the presence of doxycycline which can be misleading.

2. DDMAC – No objections.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

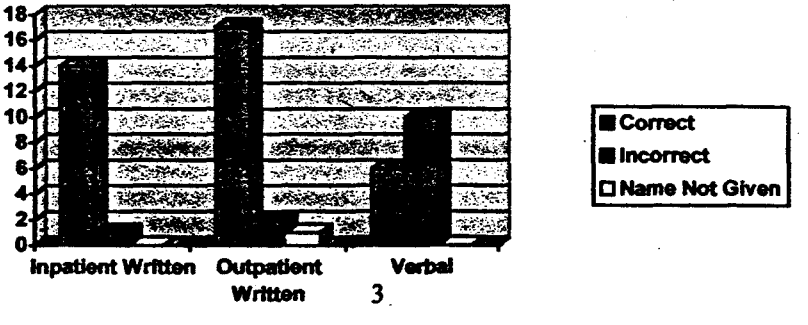
The studies conducted by OPDRA involved ninety-two health professionals comprised of pharmacists, physicians, and nurses within FDA to determine the degree of confusion of Clindoxyl Gel with other drug names due to the similarity in handwriting and verbal pronunciation of the name. Written prescriptions, consisting of (known/unknown) drug products and a prescription for Clindoxyl Gel were scanned into a computer and were then delivered to a random sample of the participating health professionals via e-mail. In addition, verbal orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted	Name Not Given
Inpatient Written	30	15 (50 %)	14 (93.3 %)	1 (6.7 %)	0 (0 %)
Outpatient Written	31	20 (64.5 %)	17 (85 %)	2 (10 %)	1 (5 %)
Verbal	31	16 (51.6 %)	6 (37.5 %)	10 (62.5 %)	0 (0 %)
Total	92	51 (55.4 %)	37 (72.5 %)	13 (25.5 %)	1 (2 %)



C. SAFETY EVALUATOR RISK ASSESSMENT

According to our searches, the proposed proprietary name, Clindoxyl Gel, poses no significant safety risk due to the lack of potential confusion with existing product names. However, the stem, "doxy", in Clindoxyl seems misleading since it could imply that this drug contains clindamycin and doxycycline. This stem is used in doxycycline product names such as Doxy 100 and Doxy 200. On the other hand, this stem is not used exclusively to describe doxycycline. For example, doxylamine succinate is an antihistamine.

According to the results of the verbal and written analysis studies, the majority of the participants (thirty-seven out of fifty-one) correctly interpreted the proposed proprietary name. Furthermore, the majority of the incorrect responses were misspelled/phonetic variations of the drug name. Moreover, the responses did not overlap with any existing approved drug products. In addition, the potential concerns regarding drug marketing and promotion related to the proposed name produced no objections by DDMAC. Therefore, there is insufficient evidence at this time to conclude that there is a safety risk of name confusion and to render the proposed proprietary name, Clindoxyl Gel, objectionable.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container label, carton and insert labeling of Clindoxyl Gel, OPDRA has attempted to focus on safety issues relating to possible medication errors. OPDRA has reviewed the current container label, carton labeling, and the package insert and has identified several areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL

1. We recommend revising the established name and strength to read:

   CLINDOXYL™ GEL
   (Clindamycin 1% and Benzoyl Peroxide 5% Gel)

   In addition, we recommend increasing the prominence of the proprietary and established names.

   *Note: The phosphate equivalency will be reflected in the "Each gram contains..." statement.

2. According to the back panel, the product should be stored in a "cold place, preferably in a refrigerator, between 2° and 8° C (36° and 46° F)." However, the next item on the label states, "Store at controlled room temperature between 15° and 30° C (59° and 86° F)" to the pharmacist. These two different storage temperature ranges could be confusing to the user. We recommend revising the label to minimize the confusion.

3. On page 028A, we recommend revising the phrase, "Professional Sample," to read:

   Professional Sample- Not for Sale

B. CARTON LABELING

1. On page 030A, the net quantity and the strength are separated by a dash (e.g. 20 – 5 gram). We

recommend revising the labeling so that the strength and the net quantity are separated and easily distinguishable.

2. See comments under CONTAINER LABEL.

IV. RECOMMENDATIONS:

A. OPDRA has no objections to the use of the proprietary name, Clindoxyl Gel.

B. OPDRA recommends the above labeling revisions that might lead to safer use of the product.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Lauren Lee, Pharm.D. at 301-827-3243.

/S/

Lauren Lee, Pharm.D.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/

Jerry Phillips, RPh
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

APPEARS THIS WAY
ON ORIGINAL

CC:

NDA: 50-741
Office Files
HFD-540; DivFiles; Olga Cintron, Project Manager
HFD-540; Jonathan Wilkin, Division Director
HFD-042, Patricia Staub, Regulatory Review Officer, DDMAC (Electronic Only)
HFD-440; Mary Dempsey, Project Manager, DDRE II, OPDRA (Electronic Only)
HFD-400; Sammie Beam, Project Manager, Medication Errors, OPDRA (Electronic Only)
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (Electronic Only)
HFD-002; Mac Lumpkin, Deputy Center Director for Review Management
(Electronic Only)

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*: OPDRA/Sammie Beam			FROM: Olga Cintron, DDDDP, HFD-540	
.TE **July 24, 2000.**	IND NO.	NDA NO. **50-741**	TYPE OF DOCUMENT **Labeling amendment**	DATE OF DOCUMENT **July 14, 2000.**
NAME OF DRUG Clindoxyl Gel	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG **Anti -bacterial**	DESIRED COMPLETION DATE **August 6, 2000.**

NAME OF FIRM: Stiefel

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*: Annual Report
- ☐ **Tradename evaluation**

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
TYPE A OR B NDA REVIEW END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISION RICK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

Attached is a review from OPDRA for Clindoxyl Gel, NDA 50-741. Mock up copies of the carton and container labeling were received on July 17th, 2000. Our labeling day is scheduled for August 7, 2000. The User Fee date is September 6, 2000. Your comments are appreciated. Thank you.

SIGNATURE OF REQUESTER Olga Cintron	METHOD OF DELIVERY (Check one) E-MAIL XX☐ HAND
GNATURE OF RECEIVER	SIGNATURE OF DELIVERER

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 4/13/2000	DUE DATE: 6/15/2000	OPDRA CONSULT #: 00-0123

TO:

Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
(HFD-540)

THROUGH:

Olga Cintron
Project Manager
(HFD-540)

PRODUCT NAME:	MANUFACTURER:
Clindoxyl Gel (Clindamycin 1% and Benzoyl Peroxide 5% Gel) NDA #: 50-741	Stiefel Laboratories, Inc.

SAFETY EVALUATOR: Lauren Lee, Pharm.D.

OPDRA RECOMMENDATION:
OPDRA has no objections to the use of the proprietary name, Clindoxyl Gel. See the checked box below.

FOR NDA/ANDA WITH ACTION DATE BEYOND 90 DAYS OF THIS REVIEW
This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from the signature date of this document. A re-review request of the name should be submitted via e-mail to "OPDRAREQUEST" with the NDA number, the proprietary name, and the goal date. OPDRA will respond back via e-mail with the final recommendation.

FOR NDA/ANDA WITH ACTION DATE WITHIN 90 DAYS OF THIS REVIEW
OPDRA considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary names/NDA's from this date forward.

☒ FOR PRIORITY 6 MONTH REVIEWS
OPDRA will monitor this name until approximately 30 days before the approval of the NDA. The reviewing division need not submit a second consult for name review. OPDRA will notify the reviewing division of any changes in our recommendation of the name based upon the approvals of other proprietary names/NDA's from this date forward.

/S/

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: (301) 827-3242
Fax: (301) 480-8173

/S/ 6/21/00

Peter Honig, MD
Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(ODS; HFD-400)

DATE RECEIVED: March 21, 2002	**DUE DATE:** May 21, 2002	**ODS CONSULT #:** 00-0123-01

TO: Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH: Vickey Lutwak
Project Manager
HFD-540

PRODUCT NAME: **Clindoxyl Topical Gel** (Clindamycin 1% and Benzoyl Peroxide 5% Gel) **NDA:** 50-741	**NDA SPONSOR:** Stiefel Laboratories

SAFETY EVALUATOR: Denise P. Toyer, Pharm.D.

SUMMARY: In response to a consult from the Division of Dermatologic and Dental Drug Products (HFD-540), the Division of Medication Errors and Technical Support (DMETS) conducted a re-review of the proprietary name Clindoxyl Topical Gel. The proprietary name was reviewed and found acceptable in June 2000 (OPDRA consult # 00-0123).

DMETS RECOMMENDATION: Upon further review, DMETS reverses its initial decision and does not recommend the use of the proprietary name "Clindoxyl Topical Gel."

Carol Holquist, R.Ph.
Deputy Director
Division of Medication Errors and Technical Support
Phone: (301) 827-3242
Fax: (301) 443-5161

Jerry Phillips, R.Ph.
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration