Research in Dermatology

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

August 8, 2000

Jonathan K. Wilkin, M.D.
Director
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

AMENDMENT
BC

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

Dear Dr. Wilkin:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 29 June 2000 telephone request for additional stability data to support the use of [redacted]: Clindamycin Phosphate, USP drug substance in the finished product, Clindoxyl™ Gel.

We are here providing six (6) month accelerated stability data generated on three (3) lots of finished product produced with Clindamycin Phosphate supplied by [redacted] as requested.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Senior Manager
Regulatory Affairs

ORIGINAL

ORIGINAL

EC

Research in Dermatology

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

CENTER FOR DRUG
REC'D
JUL 17 2000
MEGA DOC RM
EVALUATION AND RESEARCH

July 14, 2000

Jonathan K. Wilkin, M.D.
Director
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™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide)

Dear Dr. Wilkin:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 7 July 2000 telephone request for draft mock-up labeling for the individual container carton and tube.

We are here providing the requested draft mock-up labeling for the 45 gram trade size and the 5 gram professional sample.

Please note that the individual tube may be screened or labeled. Copy presentation will not change regardless of process.

Also please note that we have modified the format specific to the 5 gram professional sample carton/packer to enhance readability.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Senior Manager
Regulatory Affairs

ORIGINA

BM

Research in Dermatology

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

July 14, 2000

Jonathan K. Wilkin, M.D.
Director
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™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide)

Dear Dr. Wilkin:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 26 June 2000 telephone request for a financial disclosure certification for designated studies and for information specific to the assessment of safety and effectiveness of Clindoxyl Gel in pediatric patients.

We are here providing the requested information specific to financial disclosure and the assessment of safety and effectiveness in pediatric patients.

Following please find completed form FDA 3454 specific to Study No. 156: A Multicenter, Double-Blind Clinical Comparison of the Efficacy and Safety of Clindoxyl Gel, Clindamycin Gel, and Benzoyl Peroxide Gel in the Once Daily Treatment of Acne Vulgaris for 11 Weeks; Study No. 158: A Multicenter, Double-Blind Clinical Comparison of the Efficacy and Safety of Clindoxyl Gel, Clindamycin Gel, Benzoyl Peroxide Gel, and Vehicle Gel in the Once Daily Treatment of Acne Vulgaris for 11 Weeks; as well as Study No. 157: A Clinical Evaluation of the Potential of Clindoxyl Gel for Inducing Contact Sensitization.

Also following please find pediatric use information in accordance with the provisions of 21 CFR 314.55.

We are here requesting a partial waiver of the requirements of assessment for pediatric use with respect to the specific pediatric age groups including birth up to 12 years (neonates, infants and children) in accordance with the provisions of 21 CFR 314.55(c)(3).

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Senior Manager
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FA[illegible]

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUL 03 2000
MEGA DOC RM

NDA ORIG AMENDMENT

June 29, 2000

Jonathan K. Wilkin, M.D.
Director
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

BM

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

Dear Dr. Wilkin:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 26 June 2000 telephone request specific to providing a tabulation of the number of subjects and severity of the local effects of erythema, peeling, burning and dryness for each treatment group for studies #156 and #158; financial disclosure certification; and information specific to the assessment of safety and effectiveness in pediatric patients.

We are here providing the requested tabulation of the number of subjects and severity of the local effects of erythema, peeling, burning and dryness for each treatment group for studies #156 and #158 via this Telephone Amendment to the NDA.

Information specific to financial disclosure and the assessment of safety and effectiveness in pediatric patients will follow at an early date.

ORIGINAL

Please note that we have provided the incidence of the local effects, erythema, peeling, burning and dryness for during treatment, as requested, and, due to the relative incidence prior to treatment – we have also provided the incidence of the referenced local effects before treatment.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr

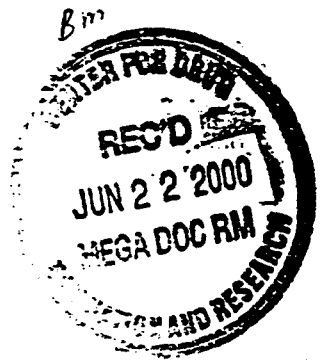
Mary Jane Carr
Senior Manager
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Research in Dermatology

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

AMENDMENT



June 20, 2000

Jonathan K. Wilkin, M.D.
Director
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™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide)

Dear Dr. Wilkin:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 20 June 2000 telephone request specific to providing a tabulation of the overall incidence and maximum severity of the local effects of erythema, dryness, burning and peeling for studies #156 and #158.

We are here providing the requested information via this Telephone Amendment to the NDA.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Senior Manager
Regulatory Affairs

DUPLICATE

Research in Dermatology

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

MAY 04 2000

May 2, 2000

Jonathan K. Wilkin, M.D.
Director
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

NDA ORIG AMENDMENT

BC

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

Dear Dr. Wilkin:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 27 April 2000 facsimile communication requesting additional chemistry related information.

We are here responding to FDA's 27 April communication via this Facsimile Amendment to the NDA.

Our response is numerically keyed to FDA's comments for ease of review. Additional supporting data is also included in the submission as required.

FDA Comment

1. It is unclear in the submitted CMC documents whether [redacted] clindamycin phosphate was the only clindamycin phosphate used in all Phase III pivotal clinical trials and preclinical studies. Please provide a summary table listing which clinical trials and preclinical studies used either the [redacted] clindamycin phosphate by lot or batch number and by formulation numbers.

Stiefel Response

Please find enclosed a summary table referencing the source of clindamycin phosphate for all clinical and preclinical trials included in the application.

ORIGINAL

FDA Comment

2. An explanation why —— the primary clindamycin phosphate supplier, is being replaced with the —— material.

Stiefel Response

As of May 1998, —— discontinued production of clindamycin phosphate drug substance.

However, as noted in our 13 April 2000 Telephone Amendment, we have retained a quantity of —— clindamycin phosphate drug substance sufficient to produce approximately six (6) production batches of Clindoxyl Gel.

All subsequent commercial production of Clindoxyl Gel will utilize clindamycin phosphate, USP produced by ——

FDA Comment

3. A table listing —— clindamycin phosphate specifications which include specific impurity limits. These data appeared scattered throughout the submission and difficult to identify.

Stiefel Response

Enclosed please find Raw Material Tests and Specifications for Clindamycin Phosphate produced by —— Pharmaceuticals. (Please also refer to Volume 2 of 32; page 058 of our March 3, 2000 Major Amendment to NDA 50-741).

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr

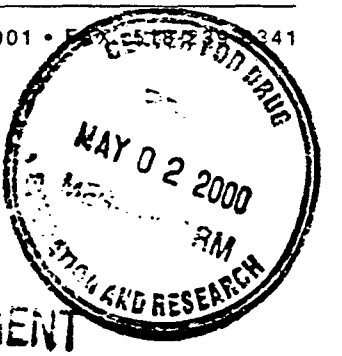
Mary Jane Carr
Senior Manager
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • F[illegible]341

May 1, 2000



Director
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

NDA [illegible] AMENDMENT

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

BS

Dear Sir/Madam:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 26 April 2000 facsimile request for the submission of Statistical Reports of Studies 156 and 158 in electronic format, and SAS data sets, data dictionary, and programs for the primary efficacy analysis in referenced studies.

We are here responding to FDA's 26 April communication via this Facsimile Amendment to the NDA.

Enclosed please find the above requested information, on diskette in PC-SAS, unzipped transfer format, as requested.

Please note that a hard copy is provided specific to an Index of Files and Stiefel Research Institute, Inc. Research Guideline for Clinical Data Entry for each of the above referenced studies. along with other pertinent information.

We look forward to your review.

ORIGINAL

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Mary Jane Carr
Senior Manager
Regulatory Affairs

001

Research in Dermatology

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

April 13, 2000

Director
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

ORIG
NDA ~~SUPPL~~ AMENDMENT

BC

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

Dear Sir/Madam:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 12 April 2000 telephone request for clarification on the source of supply specific to clindamycin phosphate, USP drug substance.

We here confirm initial production batches of Clindoxyl Gel will utilize clindamycin phosphate, USP drug substance produced - prior to their May 1998 discontinuance - by —

—

As a matter of interest, we have purchased a quantity of — clindamycin phosphate, USP to support — of Clindoxyl Gel.

All subsequent commercial production of Clindoxyl Gel will utilize clindamycin phosphate, USP produced by —

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

ORIGINAL

Mary Jane Carr
Mary Jane Carr
Senior Manager
Regulatory Affairs

Research in Dermatology

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

April 4, 2000

NDA ORIG AMENDMENT

Ms. Olga Cintron
Project Manager
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, Room N248
Rockville, MD 20850

BL

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

Dear Ms. Cintron:

Reference is made to our New Drug Application specific to Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 3 April 2000 telephone request for draft labeling on diskette in Word format.

We are here providing draft labeling on diskette in Word format, as requested.

Please note that a hard copy of subject labeling is also provided.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

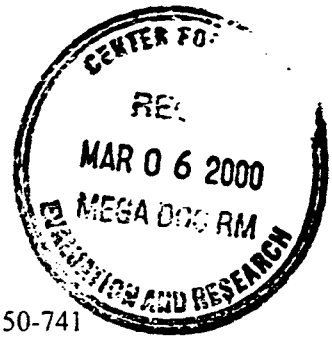
ORIGINAL

Mary Jane Carr
Senior Manager
Regulatory Affairs

Research in Dermatology

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

March 3, 2000



Jonathan K. Wilken, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane, HFD-540
Rockville, MD 20857

NDA ORIG AMENDMENT

Az

RE: MAJOR AMENDMENT to NDA 50-741
Clindoxyl Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% bezoyl peroxide)

Dear Dr.Wilken:

Reference is made to our New Drug Application dated May 3, 1996, received at FDA May 14, 1996, specific to Clindoxyl Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's not approvable communications dated May 14, 1997 and January 30, 1998 and to the February 20, 1998 telephone communication specific to corrective actions required for subject NDA.

Reference is also made to FDA's 9 March 1998 (draft) communication which restated the essential elements of the above communications.

We are pleased to respond to the above communications via this MAJOR AMENDMENT and recognize the flexibility and discretion FDA applied in the "Application Integrity Policy" by allowing us to proceed with the several studies referenced herein substantially as discussed during our 12 February 1998 meeting with representatives of The Office of the Commissioner, The Office of the Chief Counsel, The Center for Drug Evaluation and Research and numerous additional Office and Division Staff.

Our response is generally keyed to the March 9, 1998 communication and includes, as appropriate, additional points referenced only in the May 14, 1997 communication.

A. Chemistry

FDA Comment

1. An acceptable supplier of clindamycin phosphate should be identified and referenced either by AADA, or DMF, including the appropriate letters of authorization. Otherwise, the Sponsor is requested to submit full chemistry, manufacturing, and control (CMC) information pertaining to the manufacturing of bulk clindamycin phosphate.

Stiefel Response
We are submitting required documentation to support the use of clindamycin phosphate supplied by ——.

We are also submitting required documentation to support the use of clindamycin phosphate, USP supplied by an alternate supplier. ——

FDA Comment
2. ——, stability data for each of three production lots of Clindoxyl Gel, as stored under ambient (25°C/60% RH) condition. ——, accelerated stability data (40°C/75%RH) is also requested. These stability studies can be run concurrently with nonclinical and clinical studies however, the Sponsor is advised of the definite risk they assume by initiating a pivotal trial before finalizing CMC stability issues.

Stiefel Response
Following please find available accelerated (25°C/60%RH) and long-term (6°C/ambient RH) stability data for each of three (3) production lots of Clindoxyl Gel which were produced with clindamycin phosphate supplied by ——.

In addition – please find available accelerated and long-term stability data for each of three (3) production lots of Clindoxyl Gel which were produced with clindamycin phosphate supplied by ——.

As a point of clarification specific to accelerated stability – please note that the predominant storage condition for Clindoxyl Gel is under refrigerated conditions, with post-dispensing storage at 15° to 30°C. We therefore consider 25°C/60%RH to be the predominant accelerated station. We have, however, included 30°C and 40°C data in the interest of completeness.

Also please note that all of the above referenced data is specific to Master Formula (MF) —, which is formulated to contain —— of the preservative methylparaben as originally communicated to FDA in our March 9, 1998 Information Amendment to IND —— Submission Serial No. 009.

Information concerning process control, in-process control and antimicrobial preservative effectiveness test data is also submitted.

FDA Comment
3. Provide specification 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.

Stiefel Response
The regulatory specifications now incorporate limits for all known degradation products of clindamycin in the presence of benzoyl peroxide in the gel formulation.

Specifically —

Spectra for the principle degradation products referenced above, as well as for — are provided.

FDA Comment

4. Submit the chemical degradation pathway for impurities of Clindoxyl Gel.

Stiefel Response

Impurities that exceed or may exceed the reporting threshold of 0.1% of drug substance include —

Degradation pathways are here submitted. A development report specific to — is also submitted.

Very recent development studies suggest that a — tentatively identified as —, appears in some accelerated samples. If confirmed, information on subject degradate will be submitted.

In a related issue, limits for related compounds were established based on the Benzoyl Peroxide Gel, USP monograph while limits for related substances were established taking into account the end-product (Gel) specifications here referenced.

B. Clinical

FDA Comment

1. Conduct a single multicentered, adequate, well-controlled, study consisting of three arms: Clindoxyl Gel vs. clindamycin vs. benzoyl peroxide, to demonstrate the superiority of Clindoxyl Gel over both clindamycin alone and benzoyl peroxide alone.

Stiefel Response

We have conducted and here submit data from two multi-centered, adequate and well-controlled studies with Clindoxyl Gel produced with clindamycin phosphate supplied by —. Each study, in our judgement, meets the proof of effectiveness criteria generally established by FDA.

Sensitization data is also submitted which confirms that Clindoxyl Gel demonstrated a sensitization potential comparable to single-entity benzoyl peroxide products.

C. Pharmacology/Toxicology

FDA Comment

1. Conduct a 12-week dermal toxicity study, preferably in minipigs, with the final formulation stored for the allowed storage period. This study may be conducted concurrently with the requested clinical study.

Stiefel Response
Aged and non-aged Clindoxyl Gel and vehicle gel were applied to Minipigs — Yucatan pigs for 90 days. The results of the study submitted herein suggest that Clindoxyl Gel which has been aged for 60 days is nontoxic.

D. Biopharmaceutics

FDA Comment
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.

Stiefel Response
We have conducted an in vitro assessment of the percutaneous absorption of both clindamyicn and benzoyl peroxide from Clindoxyl Gel, Cleocin-T Solution and a single entity benzoyl peroxide product.

Data from the here submitted study conducted by [redacted] suggests that the percutaneous absorption of clindamycin and benzoyl peroxide from Clindoxyl Gel does not differ materially from the percutaneous absorption observed with Cleocin-T Solution and with a single entity benzoyl peroxide product.

A study to assess the percutaneous absorption of Clindoxyl Gel in man has also recently been performed and preliminary results are here submitted. The study included Clindoxyl Gel (UK formula – substantially identical to the US formula) and Dalacin-T Solution (substantially identical to Cleocin-T Solution).

Available results suggest that the benzoyl peroxide component of the combination product Clindoxyl Gel does not appear to increase the absorption of clindamycin compared to a single entity product. The absorption of clindamycin sulfoxide was negligible for both products (Clindoxyl and Dalacin).

E. Microbiology

FDA Comment
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 organisms. As written, it would not be possible to meet these criteria.

Stiefel Response
The method "Microbial Quality of Nonsterile Products (BT-11)" term "any other etiologic agent" has been modified to include more definitive terminology and is here submitted.

FDA Comment
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.

Stiefel Response
We commit to performing antimicrobial preservative effectiveness testing on the first three production lots as requested. Subject testing has been made a part of the submitted stability protocol.

F. Phase 4

FDA Comment
1. If Clindoxyl Gel is unstable under conditons of storage or use, the Sponsor is requested to conduct photocarcinogenicity studies with the proposed formulation stored for its allowed storage period.

2. Clindoxyl Gel should either be labeled as a promoter of carcinogenesis (based on literature for benzoyl peroxide) or the Sponsor is requested to conduct an alternative or traditional dermal carcinogenicity study with the final formulation to inform the label.

Stiefel Response
We understand that the issue of potential carcinogenicity and/or photocarcinogenicity of benzoyl peroxide has not been finally resolved and that Phase 4 studies may be needed.

We have as an interim measure, as with all benzoyl peroxide products, incorporated required sun exposure warnings in the proposed labeling.

We look forward to your timely review of this submission.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carl, 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

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAR 06 2000
MEGA DOC RM

APPLICANT INFORMATION

NAME OF APPLICANT: Stiefel Laboratories, Inc.	DATE OF SUBMISSION: March 3, 2000
TELEPHONE NO. *(Include Area Code)*: (305) 443-3800	FACSIMILE (FAX) Number *(Include Area Code)*: (305) [illegible]
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 255 Alhambra Circle, Suite 1000 Coral Gables, FL 33134	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE: 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)*: Clindamycin Phosphate and Benzoyl Peroxide	PROPRIETARY NAME *(trade name)* IF ANY: Clindoxyl™ Gel
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*: Methyl 7-chloro-6,7,8-trideoxy-6-[(1-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)*: None
DOSAGE FORM: Gel	STRENGTHS: Clindamycin Phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide
ROUTE OF ADMINISTRATION: Topical	

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

APPLICATION INFORMATION

APPLICATION TYPE (check one): XX NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94) ☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE: XX 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 XX 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 communications dated March 9, 1998 (draft), May 14, 1997, and January 30, 1998.

PROPOSED MARKETING STATUS (check one): XX PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED: 32 THIS APPLICATION IS: XX 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

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

See attached

This application contains the following items: *(Check all that apply)*	
XX	1. Index
XX	2. Labeling (check one) ☒ Draft Labeling ☐ Final Printed Labeling
XX	3. Summary (21 CFR 314.50 (c))
XX	4. Chemistry section
XX	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)
XX	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
XX	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))
XX	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)
XX	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
XX	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
XX	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)
XX	16. Debarment certification (FD&C Act 306 (k)(1))
XX	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	2/3/00
ADDRESS *(Street, City, State, and ZIP Code)* Route 145 Oak Hill, New York 12460		Telephone Number (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 and 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
200 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.

FORM FDA 356h (7/97)

CENTER FOR DRUG
REC'D
MAY 14 1996
CDR
EVALUATION AND RESEARCH

Research in Dermatology

STIEFEL LABORATORIES, INC., OAK HILL, NY 12460 • TEL. 518-239-6901 • FAX. 518-2

May 3, 1996

CENTER FOR DRUG
REC'D
MAY 15 1996
HFD
EVALUATION AND RESEARCH

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

RE: NDA 20,722
Clindoxyl™ Gel

Dear Sir:

We are here submitting an Application to Market a New Drug for Human Use in accordance with the provisions of 21 CFR §314.50.

Enclosed please find a completed form FDA 356h and supporting documentation for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Please direct all communications concerning this application to:

Mr. William A. Carr, Inc.
Vice-President Regulatory
Affairs and Quality Assurance
Stiefel Laboratories, Inc.
Route 145, Oak Hill, NY 12460

Tel: (518)239-6901
Fax: (518)239-8402

We look forward to FDA's timely review of this application.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:cgw

ORIGINAL

Research in Dermatology

NEW CORRESPONDENCE

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

12 June 1996

CENTER FOR DRUG
REC'D
JUN 2 1 1996
HFD-
EVALUATION AND RESEARCH

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:

We certify that to the best of our knowledge Stiefel Laboratories, Inc., and Stiefel Research Institute, Inc., have not and will not use in any capacity the service of a person debarred under subsection (a) or (b) [Section 306(a) or (b)] of the Federal Food, Drug and Cosmetic Act, in support of this - or any other - New Drug Application.

Further, we certify that to the best of our knowledge neither Stiefel Laboratories, Inc., or Stiefel Research Institute, Inc., nor any affiliated persons have been convicted under 306(a) or (b).

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

ITEMS COMPLETED
ORIGINATION
LETTER ☐ N.A.I. ☐ MEMO
DATE

CORPORATE OFFICES: 255 ALHAMBRA CIRCLE, SUITE 1000, CORAL GABLES, FLORIDA 33134
ATLANTA, GEORGIA • RENO, NEVADA • BUENOS AIRES, ARGENTINA • EPPING, AUSTRALIA • BRUXELLES, BELGIUM • GUARULHOS, BRAZIL • MONTREAL, CANADA • SANTIAGO, CHILE
BOGOTA, COLOMBIA • HIGH WYCOMBE, ENGLAND • NANTERRE, FRANCE • OFFENBACH AM MAIN, GERMANY • ATHENS, GREECE • SLIGO, IRELAND • MILAN, ITALY
TOKYO, JAPAN • SEOUL, KOREA • SAN JUAN DEL RIO, MEXICO • CASABLANCA, MOROCCO • LAHORE, PAKISTAN • MANILA, PHILIPPINES • AMADORA, PORTUGAL
BAYAMÓN, PUERTO RICO • JURONG, SINGAPORE • JOHANNESBURG, SOUTH AFRICA • MADRID, SPAIN • ZURICH, SWITZERLAND • TAIPEI, TAIWAN • BANGKOK, THAILAND

Research in Dermatology

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

NEW CORRESPONDENCE

CENTER FOR DRUG
REC'D
JUN 2 1 1996
HFD-
EVALUATION AND RESEARCH

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

CSO ACTION
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

ORIGINAL

Research in Dermatology

NEW CORRESPONDENCE

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

Noted. SW 7/11/96
What kind of amendment?
NAD

14 June 1996

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

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

Dear Sir/Madam:

We are here submitting a hard copy of our Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) (facsimile transmission - dated 13 June 1996).

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

CENTER FOR DRUG
REC'D
JUN 18 1996
HFD.
EVALUATION AND RESEARCH

ORIGINAL

Research in Dermatology

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

BC

NDA ORIG AMENDMENT

19 June 1996

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

RE: AMENDMENT
NDA 50-741

Dear Sir/Madam

We are here submitting an Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) to provide Antimicrobial Preservative Effectiveness 'raw data' for the above referenced product in accordance with FDA's 18 June 1996 telephone request.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

REVIEWS COMPLETED

CSO ACTION
☐ LETTER ☐ N.A. ☐ MEMO

CSO INITIALS DATE

001

ORIGINAL

Research in Dermatology

NEW CORRESPONDENCE

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

24 June 1996

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

RE: NDA 50-741

Dear Sir/Madam:

We confirm that Stiefel Laboratories, Inc. and Stiefel Research Institute, Inc. referenced in NDA 50-741 relative to the manufacture and testing, respectively, of Clindoxyl™ Gel are ready for inspection by the U.S. Food and Drug Administration.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

DATE

ORIGINAL

Research in Dermatology

NEW CORRESPONDENCE

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

24 June 1996

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

REVIEWS COMPLETED
CSO ACTION
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

RE: AMENDMENT
NDA 50-741

Dear Sir/Madam

We are here submitting an Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) specific to FDA's 24 June 1996 telephone request for confirmation of the inspectional readiness of our Oak Hill, New York facilities.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 25 1996

ORIGINAL

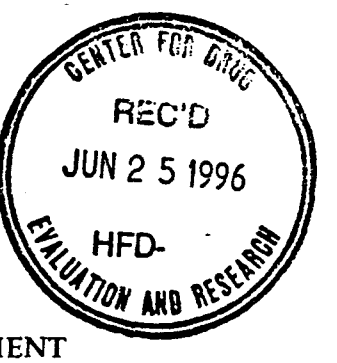
Research in Dermatology

NEW CORRESPONDENCE

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

24 June 1996

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



RE: AMENDMENT
NDA 50-741

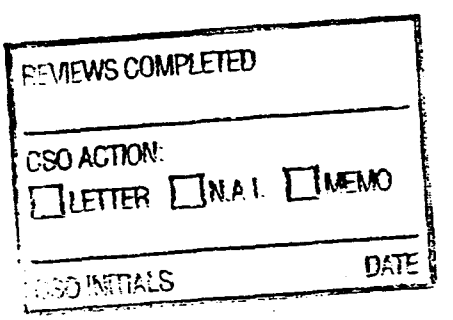
Dear Sir/Madam:

This letter is to confirm that a true copy of our Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) specific to FDA's 24 June 1996 telephone request has been submitted to Buffalo District Office, U.S. Food and Drug Administration, as specified at 21 CFR §314.60(c).

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

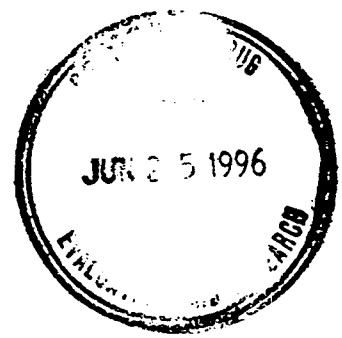


ORIGINAL

Research in Dermatology

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

NEW CORRESPONDENCE 24 June 1996



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

RE: AMENDMENT
NDA 50-741

Dear Sir/Madam

We are here submitting a 'hard copy' of our facsimile communication dated 24 June 1996 which consisted of an Amendment to our New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) specific to FDA's 24 June 1996 telephone request for confirmation of the inspectional readiness of our Oak Hill, New York facilities.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

ORIGINAL

Research in Dermatology

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

REC'D
AUG 0 2 1996
HFD
EVALUATION AND RESEARCH

August 1, 1996

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

RE: Amendment to NDA 50-741
Clindoxyl™ Gel

Dear Sir:

We are here submitting an amendment to our pending NDA for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and benzoyl peroxide 5%).

Reference is made to FDA's 24 July 1996 communication specific to the above referenced NDA.

Reference is also made to FDA's 30 July 1996 telephone communication requesting a partial response upon completion of each comment relative to point 4 of the 24 July communication.

This amendment is specific to point 4 of the 24 July communication - WP text on diskette.

Please find following the diskette with WP text of the technical reports: Vol. 1.18 pp 008-029; vol 1.20 pp. 010-040; vol 1.23 pp. 011-043.

Our response to points 1 through 3, and the remainder of point 4 will follow under separate cover when available.

We look forward to your timely review of this submission.

RECEIVED
[illegible]

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

a community's solid waste management system which may include landfills, incineration, and recycling, although minimal quantities may be disposed of in the sewer system.

FDA Comment (point 4)

Total lesion count should be included as a primary efficay variable. Therefore, the applicant must provide efficacy analyses tables for the total lesion count, similar to those for inflammatory lesion count. In addition, the applicant should provide SAS (release 6.10) programs used to generate basic tables and figures. Also, diskettes with WP test of the technical reports: vol. 1.18 pp. 008-029; vol. 1.20 pp. 010-040; vol. 1.23 pp. 011-043. Moreover, the applicant should investigate why site 152B produced unexplainable efficacy results. This information should be provided to the Agency.

Stiefel Response

Total lesion count has been analyzed as requested. Please refer to vol. 2 of 4 and vol. 3 of 4 of this submission.

SAS programs are also here included. Please refer to vol. 4 of 4 of this submission.

Diskettes with WP text have been submitted to the Agency, as required (Amendment to NDA 50-741 dated August 1, 1996).

The unexplainable efficacy results of Study 152B have been thoroughly investigated, but no answer could be found as to why the results were so much different than the other 6 study sites. There were no mix ups in labeling the medications since our labeling logsheets and related monitoring and control procedures document that the medications were properly labeled. The investigator's staff provided the correct medication to each patient as documented on the Medication Log of each patient's case report form. At least two monitors were present on site at critical stages of the study (pre-investigation, at study initiation, during the middle of the study, and at the final study visit) and no protocol or other deviations were observed that would have accounted for these divergent results. This study was conducted from Fall to Winter like most other sites and had a patient population with demographics similar to other sites although the patients at site 152B did tend to have lower non-inflammatory lesion counts and a higher incidence of facial erythema at baseline than at other sites. None of the above information provides evidence of why the benzoyl peroxide products were less effective at this site. Perhaps some unknown patient or investigator bias may be involved or the results are due to chance alone.

We look forward to your timely review of this submission.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

ORIGINAL

Research in Dermatology

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

September 27, 1996

Director
Division of Dermatologic and
Dental Drug Products, FDA
9201 Corporate Blvd.
2nd Floor North
Rockville, MD 20850

NEW CORRESPONDENCE

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

Dear Sir:

Reference is made to our pending New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's 26 September 1996 telephone communication specific to the submission of labeling on diskette for the above referenced NDA.

We are here responding to FDA's 26 September communication via an Amendment to our pending NDA in accordance with the provisions of 21 CFR 314.60(a).

Please find enclosed the original 'hard copy' of draft labeling, which retains the original pagination (NDA 50-741, vol. 1.3, pp. 408-417) and labeling on diskette (WP 6.1) as requested.

Please note that graphic characters could not be incorporated into diskette format. These characters, which include individual tube layout (p. 409), individual carton layout (p. 412), and structural formulas (p. 413), are <u>not</u> included in the diskette copy.

Also as directed, the archival copy of this submission will contain only hard copy of labeling, a desk copy of this submission will contain both hard copy and diskette, and neither a review copy or a field copy is included as part of this submission.

We look forward to your timely review of this submission.

Sincerely,
STIEFEL LABORATORIES, INC.

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

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

WAC:mf

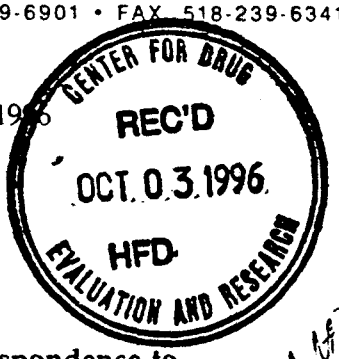
CENTER FOR DRUG
REC'D
SEP 30 1996
HFD
EVALUATION AND RESEARCH

ORIGINAL

NEW CORRESPONDENCE

Research in Dermatology

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



27 September 1996

Joseph Pierro, M.D.
Food and Drug Administration
Division of Scientific
Investigations, HFD 344-CIB
7520 Standish Place, Room 125
Rockville, MD 20855

RE: **General Correspondence to**
Clinical Investigational Branch
NDA 50-741
Clindoxyl™ Gel

10/15/96

/S/

Dear Dr. Pierro:

In accordance with your telephone request of 25 September 1996 please find following information specific to our New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Specifically, information requested, separated by key sites 150, 151B, and 152A, include the following:

List # enrolled, completed, dropped out, evaluated
List of premature withdrawals and reason
List of protocol violations
List of all adverse events
List of random code #'s and start date
Line listing of key efficacy variables

REVIEWS COMPLETED
CSO ACTION
☐ LETTER ☐ MEMO ☐ AGENDA
CSO INITIALS DATE

This correspondence is complete in one (1) volume.

Sincerely,
STIEFEL LABORATORIES, INC.

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

WAC:mjt

cc: Kevin Darryl White, M.B.A.
U.S. Food and Drug Adminitration
Cover letter

ORIGINAL

Research in Dermatology

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

NEW CORRESPONDENCE

CENTER FOR DRUG
REC'D
FEB 03 1997
MEGA DOC RM
EVALUATION AND RESEARCH

January 31, 1997

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

RE: **TELEPHONE AMENDMENT**
NDA 50-741
Clindoxyl™ Gel

Dear Sir/Madam

Reference is made to our New Drug Application, NDA 50-741, for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Reference is also made to FDA's January 24, 1997 request for information on diskette.

We are here submitting a Telephone Amendment specific to FDA's January 24 telephone request.

Please find enclosed three separate diskettes (WP 6.1) to include one diskette with clinical summary information (volume 1.1) as well as a separate diskette with clinical trial protocols (#9401, #9405, #9406) and a third diskette with unannotated package insert copy.

A total of six (6) sets of the referenced diskettes are submitted to include two "Desk Copy" sets forwarded directly to Mr. K.D. White.

This submission is complete in one (1) volume, not including copies which are also included as required.

REVIEWS COMPLETED
CSO ACTION
☐ LETTER ☐ FINAL ☐ MEMO
CSO INITIALS DATE

Sincerely,
STIEFEL LABORATORIES, INC.

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

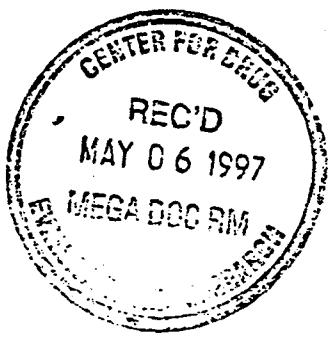
WAC:mjt

ORIGINAL

NC
NEW CORRESP

Research in Dermatology

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



May 5, 1997

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

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

Dear Sir/Madam

We are here submitting an Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide).

Enclosed please find a debarment statement - with no qualifying statements - in accordance with with FDA's 3 May 1997 telephone request.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjt

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

Research in Dermatology

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

RECEIVED FOR FILING
RECD
MAY 06 1997
MEGA DOC RM.

May 5, 1997

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

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

Dear Sir/Madam

This letter is to confirm that a true copy of our Amendment to New Drug Application for Clindoxyl™ Gel (clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide) has been submitted to Buffalo District Office in accordance with the provisions of 21 CFR 314.60(a).

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjt

APPEARS THIS WAY ON ORIGINAL

Research in Dermatology

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

May 5, 1997

RECD
MAY 06 1997

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

RE: **DEBARMENT STATEMENT**
NDA 50-741

Dear Sir/Madam

We certify that Stiefel Laboratories, Inc., and Stiefel Research Institute, Inc., have not and will not use in any capacity the service of a person debarred under subsection (a) or (b) [Section 306(a) or (b)] of the Federal Food, Drug and Cosmetic Act, in support of this - or any other - New Drug Application.

Further, we certify that neither Stiefel Laboratories, Inc., or Stiefel Research Institute, Inc., nor any other affiliated persons have been convicted under 306(a) or (b).

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjt

Number of Pages Redacted 6

❖❖❖

Confidential,
Commercial Information

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.	February 22, 2002
TELEPHONE NO. *(Include Area Code)* (305) 443-3800	**FACSIMILE (FAX) Number** *(Include Area Code)* (305) 443-3467
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):* 255 Alhambra Circle, Suite 1000 Coral Gables, FL 33134	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code telephone & FAX number)* IF APPLICABLE 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™ Topical 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: Gel	STRENGTHS Clindamycin phosphate equivalent to 1% clindamycin and 5% benzoyl peroxide	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: For treatment of the inflammatory lesions of acne vulgaris.

APPLICATION INFORMATIONT

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 7 July 2000 telephone request for draft mockups of individual container, carton and tube.

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

NUMBER OF VOLUMES SUBMITTED 5 — 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.

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

See attached.

RECEIVED
FEB 26 2002
MEGA/CDER

DUPLICATE

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))
XX	4. Chemistry section
XX	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)
XX	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))
XX	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)
XX	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))
XX	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/AGENT	TYPED NAME AND TITLE	DATE
	William A. Carr, Jr. Vice President	2/22/2002

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
200 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.

December 21, 1998

Food and Drug Administration
Central Document Room
Drug Master File Staff
12229 Wilkins Avenue
Rockville, Maryland 20852-1833
Tel. (301) 827-4210

Re: Clindamycin Phosphate - Drug Master File,
Letter of Authorization

Dear Sir or Madam:

, authorizes the FDA to reference the subject Drug Master File in support of the review of any drug applications, e.g., IND, NDA, ANDA, related Amendments and Supplements, etc., submitted by the following company where is indicated as the source of the subject drug substance:

Steifel Laboratories, Inc.
Route 145
Oak Hill, NY 12460
Regulatory Contact: Mary Jane Traver

Thank you very much for your help.

January 2, 1997

Drug Master File Staff
Food and Drug Administration
Central Document Control, Room 2-14
12420 Parklawn Drive
Rockville, MD 20852

Dear Sirs/Mesdames:

Re: Letter of Authorization
Clindamycin Phosphate USP,

hereby grants permission to the Food and Drug Administration to reference confidential information supplied within Abbreviated Antibiotic Drug Application Clindamycin Phosphate USP Non-Sterile Bulk:
Authorization is granted to support original and supplemental applications as indicated below.

SUBMITTED BY: Stiefel-Laboratories
Route 145
Oak Hill, NY 12460

PRODUCTS: Various topical Clindamycin Phosphate formulations (AADA, submission anticipated by April 1997)

This authorization is limited to information contained within the Master File mentioned above and does not permit disclosure of any confidential information to Stiefel Laboratories.

Any additional pertinent information or revisions to the Master File will be submitted to the Food and Drug Administration by It is the policy of to revise Master Files so that all statements remain accurate and current.

Sincerely,

Research in Dermatology

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

February 22, 2002

Jonathan K. Wilkin, M.D.
Director
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: **MAJOR AMENDMENT**
NDA 50-741
Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Dear Dr. Wilkin:

This letter will serve to confirm that a true copy of this Major Amendment to our New Drug Application for Clindoxyl™ Topical Gel (clindamycin - 5% benzoyl peroxide) has been submitted to Buffalo Office – New York District, U.S. Food and Drug Administration as specified at 21 CFR 314.60(c).

Sincerely,
STIEFEL LABORATORIES, INC.

William A.Carr, Jr.
Vice President

WAC:mjc

MAJOR AMENDMENT
to
New Drug Application

NDA 50-741

Clindoxyl™ Topical Gel
(clindamycin - benzoyl peroxide)

Volume 4 of 5

Stiefel Laboratories, Inc.
Coral Gables, FL 33134

Stiefel Laboratories, Inc.
NDA 50-741
Major Amendment dated February 22, 2002

Clindoxyl™ Topical Gel
(clindamycin-benzoyl peroxide)

INDEX

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-741

Stiefel Laboratories, Inc.
Attention: William A. Carr, Jr.
Vice President
255 Alhambra Circle
Suite 1000
Coral Gables, FL 33134

Dear Mr. Carr:

We acknowledge receipt on February 26, 2002 of your February 22, 2002 resubmission to your new drug application (NDA) for Clindoxyl (clindamycin/benzoyl peroxide) Topical Gel.

This resubmission contains additional information submitted in response to our September 6, 2000 action letter.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is August 26, 2002.

If you have any questions, call Victoria Lutwak, Regulatory Project Manager, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

Mary Jean Kozma-Fornaro
Supervisor, Project Management Staff
Division of Dermatologic & Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Mary Jean Kozma Fornaro
3/14/02 10:57:43 AM

APPEARS THIS WAY
ON ORIGINAL

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MAR 1 8 2002
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Research in Dermatology

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

ORIG AMENDMENT
BL

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:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin - benzoyl peroxide).

Reference is also made to FDA's March 14, 2002 telephone request for labeling in electronic format.

We are here providing the above requested labeling in electronic format (.pdf) as requested.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mcj

ORIGINAL

NDA ORIG AMENDMENT
BZ

RECEIVED
MAR 1 8 2002
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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:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin - benzoyl peroxide).

Reference is also made to FDA's March 14, 2002 telephone request for additional chemistry and safety related information.

We are here providing the above requested information via this telephone amendment to subject NDA.

Specifically, we are here providing a statement confirming that all available safety information has been submitted to FDA specific to Clindoxyl Gel, as well as updated safety statements for Canadian Clindoxyl Gel and Mexican Indoxyl Gel. Please note that both of the above referenced foreign approvals for Clindoxyl (Indoxyl) Gel relied exclusively on U.S. clinical study data generated and submitted to FDA in support of subject NDA.

We are also here providing information, to include name, address and Central File Number, for our drug substance manufacturers, benzoyl peroxide USP and clindamycin phosphate USP, and for the drug product manufacturer to facilitate required establishment inspection requests.

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

Please note that requested labeling in electronic format (.pdf) will follow under separate cover.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

ORIGINAL

Research in Dermatology

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

NEW CORRESPONDENCE
NC

RECEIVED
JUN 17 2002
MEGA/CDER

June 14, 2002

Jonathan Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Food and Drug Administration
Corporate 2, N214
9201 Corporate Blvd.
Rockville, Maryland 20850

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

Dear Dr. Wilkin:

Reference is made to our New Drug Application, NDA 50-741, for Clindoxyl™ Topical Gel (clindamycin–benzoyl peroxide) submitted on May 13, 1996.

Reference is also made to our Major Amendment to NDA 50-741 submitted on February 22, 2002 and to our May 28, 2002 teleconference with the Division of Dermatologic and Dental Drug Products (the Division). During that teleconference, the Division informed Stiefel of concerns raised in the Division of Medication Errors and Technical Support's (DMETS's) re-review of the trademark "Clindoxyl." We have prepared this submission in an effort to assist the Division as it considers the clinical relevance of these concerns.

ORIGINAL

NDA ORIG AMENDMENT
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JUL 1 0 2002
MEGA/CDER

Research in Dermatology

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

July 9, 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

RECEIVED
JUL 1 0 2002
MEGA/CDER

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

Dear Sir/Madam:

Reference is made to our New Drug Application for Clindoxyl™ Topical Gel (clindamycin - benzoyl peroxide).

Reference is also made to FDA's July 8, 2002 telephone request for container and carton labeling in electronic format.

We are here providing the above requested information via this telephone amendment to subject NDA.

Enclosed please find container and carton labeling for our 45 gram trade size and our 5 gram professional sample size units on diskette (.pdf).

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Assistant Director
Regulatory Affairs

ORIGINAL

Lutwak, Victoria L

From: mjcarr@stiefel.com
Sent: Tuesday, August 06, 2002 10:57 AM
To: lutwakv@cder.fda.gov
Subject: NDA 50-741: Clindoxyl Topical Gel (clindamycin, 1% - benzoyl peroxide, 5%)


IC Clindoxyl 45 gram 8602.pdf


tb clindoxyl 45 g 8602.pdf


pkr Clindoxyl gel ss 8602.pdf


tb Clindoxyl ss 8602.pdf

Dear Ms. Lutwak:

Reference is made to our New Drug Application specific to Clindoxyl Topical
Gel (clindamycin, 1% - benzoyl peroxide, 5%), NDA 50-741.

Reference is also made to our August 5, 2002 telephone communication specific to minor revisions to the carton, container and package insert labeling.

Specifically, we have revised our carton and container labeling to include
the following modifications:

-- the generic name has been revised to read:

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

--the generic name had been revised to:

1) increase prominence
2) italicize type
3) change color - blue

PDF files are attached specific to the draft carton and container labeling.

(See attached file: IC Clindoxyl 45 gram 8602.pdf)(See attached file: tb clindoxyl 45 g 8602.pdf)(See attached file: pkr Clindoxyl gel ss 8602.pdf)
(See attached file: tb Clindoxyl ss 8602.pdf)

The Package Insert (PI) will also be revised in accordance with the above
(with the exception of the color change since the insert is printed exclusively in black) In addition, PI modifications will be made at Line
26 and Line 27 specific to the chemical name for clindamycin phosphate. Revision to the package insert will be submitted following our scheduled conference call on Wednesday, 8/7/2002, at 2:30pm to 3:30pm, or earlier if
required.

We look forward to your review.

Sincerely,
STIEFEL LABORATORIES, INC.

Mary Jane Carr
Assistant Director
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Number of Pages Redacted 4

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Draft Labeling
(not releasable

ORIGINAL

Research in Dermatology

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

August 20, 2002

RECEIVED
AUG 22 2002
MEGA/CDER

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

NEW CORRESP

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

Dear Sir/Madam:

Reference is made to our New Drug Application for Duac™ Topical Gel (clindamycin - benzoyl peroxide).

Reference is also made to our August 20, 2002 telephone conference call with FDA Pharmacology-Toxicology Reviewer, Dr. Paul Brown, and Ms. Victoria Lutwak, Project Manager.

We are here providing a Phase 4 commitment to conduct a dermal carcinogenicity study and to evaluate the effects of the drug on UV-induced skin cancer.

These studies will be conducted in accordance with the following timeframe, as agreed during our August 20 teleconference:

- Submit protocol(s) to FDA within 4 months of receipt of NDA approval letter
- Initiate study(ies) within 6 months of FDA approval of protocol(s)
- Submit Final Report within 12 months after study(ies) completion

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

WAC:mjc

Research in Dermatology

FAX MEMORANDUM

Route 145 Oak Hill, NY 12460
Tel (518)239-6901 Fax (518)239-8402

To: Ms. Vicki Lutlak – Project Manager	From: William A. Carr, Jr.
Division of Dermatologic & Dental Drug Products, CDER, FDA	Pages: 13 Pages – Including Cover Sheet
Fax: 301-827-2091	Date: March 15, 2002
Re: NDA 50-741: Clindoxyl Topical Gel	cc:

Dear Ms. Lutlak:

Reference is made to our New Drug Application for Clindoxyl™ Gel (clindamycin - benzoyl peroxide).

Reference is also made to FDA's March 14, 2002 telephone request for additional chemistry and safety related information.

We are here providing the above requested information via this telephone amendment to subject NDA.

Please note that requested labeling in electronic format (.pdf) will follow under separate cover.

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

APPEARS THIS WAY
ON ORIGINAL

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
Office of Drug Evaluation V
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:

This letter will serve to confirm that a true copy of this Telephone Amendment to our New Drug Application for Clindoxyl™ Topical Gel (clindamycin - benzoyl peroxide) has been submitted to Buffalo Office – New York District, U.S. Food and Drug Administration as specified at 21 CFR314.60(c).

Sincerely,
STIEFEL LABORATORIES, INC.

William A. Carr, Jr.
Vice President

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. 518-239-8341

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 _____ (30 gram tubes) 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, utilized to produce Clindoxyl™ Topical Gel (clindamycin – benzoyl peroxide).

Benzoyl Peroxide, USP:

Tradename:

Manufacturing Address:

Central File Number:

Mailing Address:

Corporate Headquarters:

Clindamycin Phosphate, USP:

Manufacturing Address: [redacted]

Central File Number: [redacted]

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