

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

50-793

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

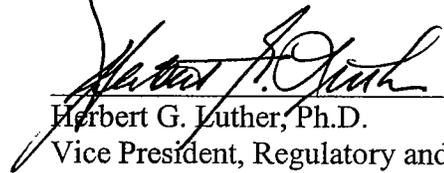


(clindamycin phosphate)
Vaginal Cream, 2.0%

EXEMPTION to 505(b) (2) PATENT FILING and CERTIFICATION REQUIREMENTS

The product of this application for which approval is being sought is exempt under 21 U.S.C. 125 (d) (2) patent filing and certification requirements since the reference listed drug, Cleocin® (Clindamycin Vaginal Cream, USP) was approved under 21 U.S.C. 507.

10/30/03
Date


Herbert G. Luther, Ph.D.
Vice President, Regulatory and Clinical Affairs

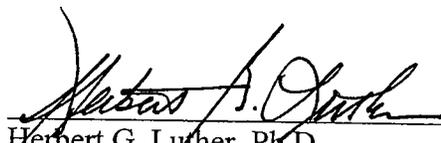


(clindamycin phosphate)
Vaginal Cream, 2.0%

PARAGRAPH I CERTIFICATION

As required by 21 C.F.R. 314.50(i)(1)(i)(A)(1), KV Pharmaceutical Company hereby certifies that in the opinion of and to the best knowledge of KV Pharmaceutical Company, patent information has not been submitted to FDA for the reference listed drug, Cleocin® (Clindamycin Vaginal Cream, USP).

10/30/03
Date



Herbert G. Luther, Ph.D.
Vice President, Regulatory and Clinical Affairs

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA# : 50-793 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: October 31, 2003 Action Date: August 31, 2004

HFD 590 Trade and generic names/dosage form: _____ ^M(clindamycin phosphate vaginal cream, 2%)

Applicant: KV Pharmaceutical Company Therapeutic Class: 4060200

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Bacterial Vaginosis

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: Range being waived; pre-menarchal females.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies *****

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments: The clinical studies included with this application conducted in adults provide sufficient evidence to allow for extrapolation to post-menarchal females for labeling purposes for the indication of bacterial vaginosis.

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Susan Peacock
Regulatory Project Manager

cc: NDA
HFD-960/ Grace Carmouze
(revised 10-14-03)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

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/s/

Susan Peacock
1/8/04 12:57:33 PM



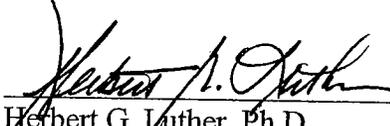
_____™ (clindamycin phosphate)
Vaginal Cream, 2.0%

DEBARMENT CERTIFICATION AND LIST OF CONVICTIONS STATEMENT

KV Pharmaceutical Company hereby certifies that it did not and will not use in any capacity the services of any person debarred under subsection (a) or (b) [section 306 (a) or (b)], in connection with this application. [Section 306 (k) (1) of the Generic Drug Enforcement Act of 1992 {21 U.S.C. 335 a (k) (1)}.]

KV Pharmaceutical Company hereby certifies that neither the applicant nor any affiliated person(s) responsible for the development or submission of this application have been convicted of any relevant crime or offense for which they are subject to debarment.

10/30/03
Date



Herbert G. Luther, Ph.D.
Vice President, Regulatory & Clinical Affairs

PRESCRIPTION DRUG USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS

KV Pharmaceutical Company
2503 South Hanley Road
St. Louis, Missouri 63144

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

YES NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

NDA 50-680

(APPLICATION NO. CONTAINING THE DATA).

2. TELEPHONE NUMBER (Include Area Code)

(314) 645-6600

3. PRODUCT NAME

(clindamycin phosphate) Vaginal Cream, 2.0%

6. USER FEE I.D. NUMBER

4630

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)

A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See item 7, reverse side before checking box.)

THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See item 7, reverse side before checking box.)

THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

YES NO

(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes 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:

Department of Health and Human Services
Food and Drug Administration
CDER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE



TITLE

Vice President, Regulatory and Clinical Affairs

DATE

10/30/03



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-793

KV Pharmaceutical
Attention: Herbert G. Luther, Ph.D.
Vice President, Regulatory and Clinical Affairs
2503 South Hanley Road
St. Louis, MO 63144-2555

Dear Dr. Luther:

Please refer to your October 30, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for clindamycin phosphate vaginal cream, 2%.

On August 24, 2004, we received your August 20, 2004 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is November 30, 2004.

If you have any questions, call Susan Peacock, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Ellen F. Molinaro, R.Ph.
Chief, Project Management Staff
Division of Special Pathogen and Immunologic
Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Ellen Molinaro
8/27/04 04:50:16 PM
NDA 50-793



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

FACSIMILE TRANSMITTAL SHEET

DATE: June 22, 2004

To: Herbert Luther, Ph.D.	From: Susan Peacock
Company: KV Pharmaceuticals	Division of Special Pathogen and Immunologic Drug Products
Fax number: 314-567-0704	Fax number: 301-827-2475
Phone number: 314-645-6600	Phone number: 301-827-2173

Subject: Labeling Questions

Total no. of pages including cover: 2

Comments:

Document to be mailed: • YES NO

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If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2127. Thank you.

Please refer to your October 30, 2003, new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for (Clindamycin Phosphate Vaginal Cream, 2%).

We are reviewing the proposed labeling for Clindamycin Phosphate Vaginal Cream, 2%, and have the following questions:

1. In the **WARNINGS** section of the label, there is the following statement:

“Mineral oil may weaken latex or rubber products such as condoms or vaginal contraceptives, diaphragms; _____

2. _____

If you have any questions, call Susan Peacock, Regulatory Project Manager, at (301) 827-2173.

Susan Peacock, Regulatory Project Manager
Division of Special Pathogen and Immunologic Drug Products

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/s/

Susan Peacock
6/22/04 02:17:31 PM
CSO

Susan Peacock
6/22/04 02:20:35 PM
CSO

MEETING MINUTES

DATE: May 19, 2004
TIME: 3:00-4:00 P.M.
LOCATION: S-426, 9201 Corporate Blvd.
NDA#: NDA 50-793
DRUG: [REDACTED] (Clindamycin Phosphate) Vaginal Cream, 2%
SPONSOR/APPLICANT: KV Pharmaceutical Company
CONTACT NAME: Herbert Luther, Ph.D.
FAX NUMBER: (314) 567-0704
PHONE NUMBER: 314) 645-6600
PROJECT MANAGER: Susan Peacock, MS
DIVISION OF: Special Pathogen and Immunologic Drug Products (DSPIDP), HFD-590
FORMAT: Teleconference

FDA PARTICIPANTS, DIVISIONS, AND TITLES:

Norman Schmuff, Ph.D., Acting Deputy Division Director, HFD-830
Mark Seggel, Ph.D., Acting Chemistry Team Leader
Dorota Matecka, Ph.D., Chemistry Reviewer
Susan Peacock, M.S., Regulatory Project Manager

KV Pharmaceutical Company:

Herbert G. Luther, PhD, Vice President, Clinical and Regulatory Affairs
Scarlett Tumulty, Regulatory Affairs Assistant

BACKGROUND:

KV Pharmaceuticals submitted a New Drug Application for [REDACTED] (clindamycin phosphate) Vaginal Cream, 2% on October 30, 2003. In the filing letter for this application, we identified potential review issues regarding the DMF due to several deficiencies. The chemistry reviewer sent a facsimile to the [REDACTED] outlining the deficiencies with the DMF. The Division wanted to speak to KV to update them on the chemistry review at this time.

DISCUSSION POINTS:

- DMF [REDACTED] referenced in the application for the [REDACTED] is a Type I DMF and the Division reviews Type 3 DMFs for [REDACTED] systems. Please submit a reference to a Type III DMF, if available.
- Please provide samples of the product. KV agreed to send samples of their product.
- Please confirm that the applicator being used is the same one used for Gynazole. KV confirmed that the [REDACTED] product using the same applicator as the Gynazole product.
- Drug Substance
 - Compliance called drug substance manufacturer earlier in the year to schedule inspection and the facility was not ready. This can be a reason for not taking an approval action.
 - Another inspection could be planned before the action date, August 31, 2004, but it may not be possible. The Division asked that KV assure that the manufacturer could be ready in [REDACTED] for an inspection.
 - KV stated that they became aware of the issues with the manufacturer of the drug substance after they had used them. KV was aware that the Division had sent the manufacturer a facsimile containing several deficiencies. KV alerted the Division to some other issues with

the drug manufacturer facility in addition to those of the Division. KV stated that they were working with the manufacturer to get them ready for inspection. KV also stated that the manufacturer would be providing responses to our deficiencies in July.

o

[REDACTED]

ACTION ITEMS:

- KV will provide the Division with samples of the product.
- KV will send a letter of authorization to a Type III DMF for [REDACTED]

Susan Peacock, Regulatory Project Manager
Minutes Preparer

Norman Schmuff, Ph.D., Acting Deputy Division Director, HFD-830
Meeting Chair

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/s/

Dorota Matecka
6/16/04 12:04:58 PM
on behalf of Norman Schmuff



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

FACSIMILE TRANSMITTAL SHEET

DATE: March 31, 2004

To: Herbert Luther, Ph.D.	From: Susan Peacock
Company: KV Pharmaceuticals	Division of Division of Special Pathogen and Immunologic Drug Products
Fax number: 314-567-0704	Fax number: 301-827-2475
Phone number: 314-645-6600	Phone number: (301) 827-2127

Subject: CMC Comments regarding NDA 50-793

Total no. of pages including cover: 3

Comments: This facsimile was reviewed by Dorota Matecka and Norman Schmuff

Document to be mailed: • YES NO

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ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND
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INFORMATION REQUEST LETTER

Dear Dr. Luther:

Please refer to your October 30, 2003, new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for ~~_____~~ (Clindamycin Phosphate Vaginal Cream, 2%).

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Please submit to your NDA the protocol and results of the antimicrobial effectiveness testing conducted on the drug product, clindamycin phosphate vaginal cream, 2%.
2. Please provide available updated stability data for the primary stability batches of the drug product.
3. Please provide the pH testing results for the batches of clindamycin phosphate vaginal cream, 2% used in the clinical studies. Please include pH testing (method and acceptance criteria) in the drug product release and stability specification as previously recommended by the Agency (via fax dated 22-Apr-2002 containing comments to your IND 62,397). Note that the proposed pH acceptance criteria for your drug product should conform to the pH requirements specified in the USP monograph for clindamycin phosphate vaginal cream.

If you have any questions, call Susan Peacock, Regulatory Project Manager, at (301) 827-2173.

Susan Peacock, Regulatory Project Manager
Division of Special Pathogen and Immunologic Drug Products

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/s/

Susan Peacock

3/31/04 09:11:54 AM



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE IV**

FACSIMILE TRANSMITTAL SHEET

DATE: January 12, 2004

To: Herbert G. Luther	From: Susan Peacock
Company: KV Pharmaceutical	Division of Special Pathogen and Immunologic Drug Products
Fax number: (314) 645-6732	Fax number: (301) 827-2475
Phone number: (314) 645-6600	Phone number: (301) 827-2127
Subject: Information Requests for NDA 50-793	

Total no. of pages including cover: 2

Comments:

Document to be mailed: • YES NO

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NDA 50-793

INFORMATION REQUEST LETTER

Dear Dr. Luther:

Please refer to your October 31, 2003 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (clindamycin phosphate) Vaginal Cream, 2%.

We are reviewing the Clinical section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Please provide final protocols for studies 01-025 and 02-005 that incorporate all amendments and changes written.
2. We were unable to locate the electronic data listings from study 01-012 (pilot study) that correspond to some of the hardcopy submissions in section 5.3.1.1, Pilot Study, Patient Listings. Specifically, these include results such as pelvic exam results (discharge color, odor, consistency, other findings), vulvovaginal itching and inflammation, return to normal discharge, whiff test for amine odor, saline wet mount for clue cells, vaginal discharge pH results and Nugent score for entry, interim and TOC visits, and if additional BV treatment was required for interim and TOC visits. If this was submitted, please describe the location in the electronic submission. Otherwise, please submit this information in electronic form.
3. Section 5.3.5.1.2, labeled "Clindamycin Study: Listing 23: Combined Extraneous Comments/Notes" is mislabeled and contains combined extraneous comments from protocol number 02-005 (placebo study). Please provide the combined extraneous comments from protocol number 01-025.

If you have any questions, please call me at (301) 827-2127.

Sincerely,

Susan Peacock, M.S.
Regulatory Project Manager
Division of Special Pathogen and Immunologic
Drug Products, HFD-590
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Susan Peacock

1/12/04 10:31:53 AM

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # **50-793**
SE8

Supplement #

SE1 SE2 SE3 SE4 SE5 SE6 SE7

Trade Name: _____
Generic Name: **clindamycin phosphate vaginal cream, 2%**
Strengths:

Applicant: KV Pharmaceutical Company

Date of Application: **October 30, 2003**

Date of Receipt: **October 31, 2003**

Date clock started after UN:

Date of Filing Meeting: **December 22, 2003**

Filing Date: **December 30, 2003**

Action Goal Date (optional):

User Fee Goal Date: **August 31, 2004**

Indication(s) requested: **Bacterial Vaginosis**

Type of Original NDA: (b)(1) _____ (b)(2) X
OR

Type of Supplement: (b)(1) _____ (b)(2) _____

NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: S X P _____
Resubmission after withdrawal? N/A Resubmission after refuse to file? N/A

Chemical Classification: (1,2,3 etc.) **5 "New Formulation or Manufacturer, Same or New Indication per draft MAPP 7500.3 version 4/18/03"**

Other (orphan, OTC, etc.) _____

User Fee Status: Paid Exempt (orphan, government) _____
Waived (e.g., small business, public health) _____

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee ID # 4630

Clinical data? YES NO, Referenced to NDA #

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?

YES NO

If yes, explain:

Does another drug have orphan drug exclusivity for the same indication? YES NO

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

Is the application affected by the Application Integrity Policy (AIP)? YES NO
 If yes, explain.

If yes, has OC/DMPQ been notified of the submission? YES NO

• Does the submission contain an accurate comprehensive index? YES NO

• Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

• Submission complete as required under 21 CFR 314.50? YES NO
 If no, explain:

• If an electronic NDA, does it follow the Guidance? N/A YES NO
If an electronic NDA, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

• If in Common Technical Document format, does it follow the guidance? N/A YES NO

• Is it an electronic CTD? N/A YES NO
If an electronic CTD, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

• Patent information submitted on form FDA 3542a? YES NO

• Exclusivity requested? YES, _____ years NO
 Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

• Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e.,

"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge"

- Financial Disclosure forms included with authorized signature? YES NO
 (Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)
- Field Copy Certification (that it is a true copy of the CMC technical section)? YES NO

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES NO
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections.
- List referenced IND numbers: IND 62,397
- End-of-Phase 2 Meeting(s)? Date(s) _____ NO
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) September 23, 2003
 NO
 If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? YES NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A YES NO
- Has DOTCDP been notified of the OTC switch application? N/A YES NO

- ___ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.
- ___ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

- ___ 21 CFR 314.50(i)(1)(ii): No relevant patents.
- ___ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.
- ___ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)
- ___ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:
 - Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?

<u>YES</u>	NO
------------	----
 - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

<u>YES</u>	NO
------------	----
 - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

N/A	<u>YES</u>	NO
-----	------------	----
 - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

<u>N/A</u>	YES	NO
------------	-----	----
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
 - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

<u>YES</u>	NO
------------	----

- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

YES NO

- EITHER
The number of the applicant's IND under which the studies essential to approval were conducted.

IND # 62,397 NO

OR

A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: December 22, 2003

BACKGROUND: NDA 50-680 for Cleocin (Clindamycin Phosphate Vaginal Cream, USP) was approved August 11, 1992. The label for Cleocin specified a dosing regimen of one applicatorful of clindamycin phosphate vaginal cream 2%, intravaginally, for 3 or 7 consecutive days. This application is seeking a shorter regimen of only one applicatorful of clindamycin phosphate vaginal cream 2% intravaginally. The KV Pharmaceutical Company program for Clindamycin 2% vaginal cream consisted of two, pivotal, Phase III clinical studies:

1. One study was randomized, double blind, placebo-controlled, parallel group, multi-center study evaluating superiority of the KV Clindamycin 2% Vaginal Cream product versus and intravaginal placebo that enrolled a total of 262 total patients.
2. The other study was a randomized, single-blind, active control, parallel group, multi-center, non-inferiority study of the KV Clindamycin 2% Vaginal Cream product versus the currently marketed CLEOCIN® Vaginal Cream 2% that enrolled 540 total patients.

The pre-NDA meeting was held on September 23, 2003.

ATTENDEES:

Renata Albrecht, Kalavati Suvarna, Philip Colangelo, Seong Jang, Cheryl Dixon, Diana Willard, Owen McMaster, Steven Gitterman, Dorothy Wawrose.

ASSIGNED REVIEWERS:

<u>Discipline</u>	<u>Reviewer (Primary/TL)</u>
Medical:	Dorothy Wawrose/Leonard Sacks
Secondary Medical:	
Statistical:	Cheryl Dixon/Karen Higgins
Pharmacology:	
Chemistry:	Dorota Matecka/Norman Schmuft
Environmental Assessment (if needed):	
Biopharmaceutical:	Seong Jang/Philip Colangelo
Microbiology, sterility:	
Microbiology, clinical (for antimicrobial products only):	Kalavati Suvarna/Shukal Bala
DSI:	
Regulatory Project Management:	Susan Peacock/Ellen Molinaro

Other Consults:

Per reviewers, are all parts in English or English translation? YES NO
If no, explain:

CLINICAL FILE X REFUSE TO FILE _____

- Clinical site inspection needed: YES NO

- Advisory Committee Meeting needed? YES, date if known _____ **NO**
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A YES NO

CLINICAL MICROBIOLOGY

FILE REFUSE TO FILE _____

STATISTICS

FILE REFUSE TO FILE _____

BIOPHARMACEUTICS

FILE REFUSE TO FILE _____

- Biopharm. inspection needed: YES **NO**

PHARMACOLOGY

NA _____ FILE REFUSE TO FILE _____

- GLP inspection needed: YES **NO**

CHEMISTRY

FILE REFUSE TO FILE _____

- Establishment(s) ready for inspection? **YES** NO
- Microbiology YES **NO**

ELECTRONIC SUBMISSION:

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

_____ The application is unsuitable for filing. Explain why:

The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

_____ No filing issues have been identified.

Filing issues to be communicated by Day 60.

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of the RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Document filing issues/no filing issues conveyed to applicant by Day 74.

 Susan Peacock
 Regulatory Project Manager, HFD-590

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

/s/

Susan Peacock
12/30/03 08:41:27 AM
CSO

Susan Peacock
12/30/03 08:44:04 AM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 50-793

KV Pharmaceutical Company
Attention: Herbert Luther, Ph.D.
Vice President, Regulatory and Clinical Affairs
2503 South Hanley Road
St. Louis, Missouri 63144

Dear Dr. Luther:

Please refer to your October 30, 2003, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [REDACTED] (clindamycin phosphate vaginal cream, 2%).

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on December 30, 2003, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues:

We find that the referenced DMF [REDACTED] is deficient. This DMF from [REDACTED] describes the synthesis of clindamycin phosphate. Among the many deficiencies, it is unclear as to who is the current U.S. agent for [REDACTED]. We have attempted unsuccessfully to contact [REDACTED] by email at [REDACTED]. We await a response from [REDACTED] indicating to whom these deficiencies should be sent. These issues must be resolved before this application can be approved.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

If you have any questions, call Susan Peacock, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

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/s/

Rigoberto Roca
12/29/03 01:54:11 PM
for Renata Albrecht, M.D.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-793

KV Pharmaceutical Company
Attention: Herbert Luther, Ph.D.
Vice-President, Regulatory and Clinical Affairs
2503 South Hanley Road
St. Louis, M.O. 63144

Dear Dr. Luther:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: **██████████** (clindamycin phosphate vaginal cream, 2.0%)

Review Priority Classification: Standard (S)

Date of Application: October 30, 2003

Date of Receipt: October 31, 2003

Our Reference Number: NDA 50-793

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on December 30, 2003, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be August 31, 2004.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

U.S. Postal Service:

Center for Drug Evaluation and Research
Division of Special Pathogen and Immunologic Drug Products, HFD-590
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

NDA 50-793

Page 2

Courier/Overnight Mail:

Food and Drug Administration

Center for Drug Evaluation and Research

Division of Special Pathogen and Immunologic Drug Products, HFD-590

Attention: Document Room

9201 Corporate Blvd.

Rockville, Maryland 20850

If you have any questions, call Susan Peacock, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Ellen F. Molinaro, R. Ph.

Chief, Project Management Staff

Division of Special Pathogen and Immunologic
Drug Products

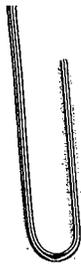
Office of Drug Evaluation IV

Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Ellen Molinaro
11/3/03 04:55:12 PM
NDA 50-793



4 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA: 50-793	Efficacy Supplement Type SE-	Supplement Number:
Drug: Clindesse™ (clindamycin phosphate) Vaginal Cream, 2%		Applicant: KV Pharmaceutical Company
RPM: Christina H. Chi, Ph.D.		HFD-590 Phone #: 301-827-2127
<p>Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p><input checked="" type="checkbox"/> Confirmed <input type="checkbox"/> and/or corrected</p>	<p>Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s):</p> <p>NDA 50-680 Cleocin (clindamycin phosphate) Vaginal Cream 2%, USP</p> <p>This application is seeking a shorter regimen of treatment than Cleocin Vaginal Cream, 2%.</p>	
❖ Application Classifications:		
• Review priority	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority	
• Chem class (NDAs only)	5	
• Other (e.g., orphan, OTC)	N/A	
❖ User Fee Goal Dates		
November 30, 2004		
❖ Special programs (indicate all that apply)		
<input checked="" type="checkbox"/> None <input type="checkbox"/> Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2		
❖ User Fee Information		
• User Fee	<input checked="" type="checkbox"/> Paid; UF ID number: 4630	
• User Fee waiver	<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify)	
• User Fee exception	<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify)	
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• This application is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
• Exception for review (Center Director's memo)		
• OC clearance for approval		

<p>❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.</p>	<p><input checked="" type="checkbox"/> Verified (Original submission dated Oct. 30, 2003; Module 1)</p>
<p>Patent</p>	<p style="background-color: #cccccc;"></p>
<ul style="list-style-type: none"> Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. 	<p><input checked="" type="checkbox"/> Verified (Original submission dated Oct. 30, 2003; Module 1)</p>
<ul style="list-style-type: none"> Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	<p>21 CFR 314.50(i)(1)(i)(A)(1) <input checked="" type="checkbox"/> Verified; exempt under 21 U.S.C. 125 (d)(2) patent filing and certification requirements 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)</p>
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<p></p>
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).</i> [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).</p> <p><i>If "Yes," skip to question (4) below. If "No," continue with question (2).</i></p> <p>(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?</p> <p><i>If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).</i></p> <p><i>If "No," continue with question (3).</i></p> <p>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of</p>	<p><input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>

receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

() Yes () No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

() Yes () No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> • Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	No
<ul style="list-style-type: none"> • Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	() Yes, Application # _____ (x) No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	NDA regulatory filing review of December 30, 2003

General Information

General Information	
Actions	
• Proposed action	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	<input type="checkbox"/> Materials requested in AP letter <input checked="" type="checkbox"/> N/A (On 11-11-2004 Sponsor sent advertising materials to DDMAC; prior to the issuance of the approval letter) <input type="checkbox"/> Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	<input checked="" type="checkbox"/> Yes, via approval e-mails <input type="checkbox"/> Not applicable
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> Press Release <input type="checkbox"/> Talk Paper <input type="checkbox"/> 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)	
• Most recent applicant-proposed labeling	<input checked="" type="checkbox"/>
• Original applicant-proposed labeling	<input checked="" type="checkbox"/>
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	<input checked="" type="checkbox"/>
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	Cleocin Labeling
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	<input checked="" type="checkbox"/>
• Reviews	DMETS review of May 17, 2004
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Yes
❖ Memoranda and Telecons	Yes
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	September 23,03
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	May 19, 2004
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	
• Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A

Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	Team Leader's memorandum: November 30, 2004
Clinical Information	
❖ Clinical review(s) (indicate date for each review)	November 29, 2004
❖ Microbiology (efficacy) review(s) (indicate date for each review)	August 1, 2004
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	Clinical review, page 46
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	January 8, 2004
❖ Demographic Worksheet (NME approvals only)	N/A
❖ Statistical review(s) (indicate date for each review)	November 30, 2004
❖ Biopharmaceutical review(s) (indicate date for each review)	August 18, 2004
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) (indicate date for each review)	November 29, 2004
❖ Environmental Assessment	N/A
• Categorical Exclusion (indicate review date)	CMC review of November 29, 2004, page 70
• Review & FONSI (indicate date of review)	N/A November 29, 2004
• Review & Environmental Impact Statement (indicate date of each review)	N/A November 29, 2004
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	6-21-2004;
❖ Facilities inspection (provide EER report)	Date completed: (x) Acceptable, September 1-2004 () Withhold recommendation
❖ Methods validation	() Completed () Requested (x) Not yet requested; will be submitted early 2005
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	November 29, 2004
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
❖ CAC/ECAC report	N/A

Appendix A to NDA/Efficacy Supplement Action Package Checklist

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).