CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 50-769

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products

Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: November 27, 2000 Number of Pages (including cover sheet) - 11

TO: Alicia Cabrelli, Regulatory Analyst
COMPANY: Dermik Laboratories, Inc.
FAX #: 484-595-2785

MESSAGE: Please find attached to this facsimile transmission, a copy of the Action Letter for NDA 50-769, Benzamycin Pak (erythromycin 3%-benzoyl peroxide 5% topical gel).

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

10 Pages have been redacted in full from this document

Reason:

_____ b(2) 'low'

__X__ b(4) CCI DRAFT LABELING AND PRODUCT PACKAGING

_____ b(4) TS

_____ b(5) Deliberative Process:
Attorney Client and Attorney Work Product Privilege

_____ b(6) Personal Privacy

_____ b(7) Law Enforcement Records

Item 13 -Patent/Exclusivity Information

1)	Active Ingredient(s):	erythromycin/benzoyl peroxide
2)	Strength(s):	3% erythromycin/5% benzoyl peroxide
3)	Trademark:	Benzamycin®
4)	Dosage Form (Route of Administration):	topical gel
5)	Application Firm Name:	Dermik Laboratories, Inc.
6)	IND Number:	12,193
7)	NDA Number:	50-769
8)	Approval Date:	N/A
9)	Exclusivity -- date first ANDA could be submitted or approved and length of exclusivity period:	Pursuant to Sections 505(c)(3)(D), 505(j)(4)(D) or 527(a) of the Federal Food, Drug and Cosmetic Act, no ANDA may be approved with an effective date which is prior to 3 years after the date of approval of this application.
10)	Applicable patent numbers and expiration date of each:	U.S. Patent No. 4,497,794, expires June 7, 2000; U.S. Patent No. 4,692,329, expires June 7, 2000; U.S. Patent No. 4,387,107, expires June 7, 2000.

11) To the best of our knowledge, each of the clinical investigations included in this application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).

A list of all published studies or publicly available reports of clinical investigations known to the applicant through a literature search that are relevant to the conditions for which we are seeking approval is attached. We have thoroughly searched the scientific literature and, to the best of our knowledge, the list is complete and accurate and, in our opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of the conditions for which we are seeking approval without reference to the new clinical investigation(s) in the application. The reasons that these studies or reports are insufficient are presented in the attachment as well.

Item 13. Patent Information

1)	Patent number	U.S. Patent No. 4,387,107
2)	Date of expiration	June 7, 2000
3)	Type of patent	drug product
4)	Name of patent owner	Dermik Laboratories, Inc.
5)	U.S. representative	Dermik Laboratories, Inc.

The undersigned declares that Patent No. 4,387,107 covers the formulation, composition, and/or method of use of Applicant's Benzamycin® (erythromycin/benzoyl peroxide) product. This product is the subject of this application for which approval is being sought.

Signed: 

Date: 2/23/99

Name: Ross J. Oehler

Title: Assistant General Counsel,
Director, US Patent & Trademark Dept.
Rhône-Poulenc Rorer Pharmaceuticals Inc.

APPEARS THIS WAY
ON ORIGINAL

Item 13. Patent Information

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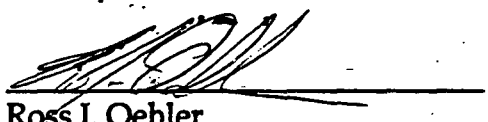
Signed: 

Date: 2/23/99

Name: Ross J. Oehler

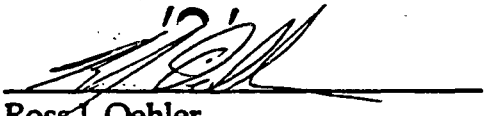
Title: Assistant General Counsel,
Director, US Patent & Trademark Dept.
Rhône-Poulenc Rorer Pharmaceuticals Inc.

APPEARS THIS WAY
ON ORIGINAL

Item 13. Patent Information

1)	Patent number	U.S. Patent No. 4,692,329
2)	Date of expiration	June 7, 2000
3)	Type of patent	drug product
4)	Name of patent owner	Dermik Laboratories, Inc.
5)	U.S. representative	Dermik Laboratories, Inc.

The undersigned declares that Patent No. 4,692,329 covers the formulation, composition, and/or method of use of Applicant's Benzamycin® (erythromycin/benzoyl peroxide) product. This product is the subject of this application for which approval is being sought.

Signed: 

Date: 2/23/99

Name: Ross J. Oehler

Title: Assistant General Counsel,
Director, US Patent & Trademark Dept.
Rhône-Poulenc Rorer Pharmaceuticals Inc.

Trade Name: Benzamycin Pak Generic Name: (erythromycin 3% - benzoyl peroxide 5% topical gel)

Applicant Name: Dermik Laboratories, Inc.

Approval Date 11/27/00

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES /_X_/ NO /___/

b) Is it an effectiveness supplement?

YES /___/ NO /_X_/

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /_X_/ NO /___/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /__/ NO /_X_/

e) Has pediatric exclusivity been granted for this Active Moiety? No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO - please indicate as such)

YES /_X_/ NO /__/

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /__/ NO /_X_/

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /_X_/ NO /__/

NDA 50-557, Benzamycin (erythromycin-benzoyl peroxide topical gel)

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_X_/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /_X_/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /_X_/

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /_X_/

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # DL-6026-9709

Investigation #2, Study # DL-6026-9723

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1, Study # DL-6026-9709 YES /___/ NO /_X_/

Investigation #2, Study # DL-6026-9723 YES /___/ NO /_X_/

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1, Study # DL-6026-9709 YES /___/ NO /_X_/

Investigation #2, Study # DL-6026-9723 YES /___/ NO /_X_/

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #1, Study # DL-6026-9709 YES /_X_/ NO /__/

Investigation #2, Study # DL-6026-9723 YES /_X_/ NO /__/

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation _____ YES /_X_/ NO /__/

Investigation _____ YES /_X_/ NO /__/

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Yes

c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X__/

/S/

Signature of Project Manager 11/27/00 Date

/S/

Signature of DDDDP Division Director 11/27/00 Date

cc: Original NDA 50-769 HFD-540 Division Files HFD-90 Mary Ann Holovac

1.8 Item 19A: Pediatric Use

Benzamycin ([redacted]rythromycin 3% and benzoyl peroxide 5% gel) was studied under the Benzamycin IND in male and female pediatric patients greater than twelve years of age. Data on this population is presented in the application. The studies conducted are consistent with the demographics of the disease population.

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements) View Word Document

NDA Number:	050769	**Trade Name:**	BENZAMYCIN ——— ENOZYL PEROXIDE 5%
Supplement Number:	000	**Generic Name:**	BENOZYL PEROXIDE 5%/ERYTHROMYCIN 3%
Supplement Type:	N	**Dosage Form:**	
Regulatory Action:	OP	**COMIS Indication:**	TOPICAL TREATMENT OF ACNE VULGARIS
Action Date:	1/27/00		

Indication # 1 Acne vulgaris.

Label Adequacy: Adequate for SOME pediatric age groups

Forumulation Needed: NEW FORMULATION developed with this submission

Comments (if any): Partial waiver for pediatric acne studies for the age group from birth through 11 years of age, under 21 CFR 314.55(c)(4)

Lower Range	Upper Range	Status	Date
0 years	11 years	Waived	11/27/00

Comments: Acne is not prevalent in the population from birth through 11 years, and this product would not represent a substantive therapeutic benefit as an acne therapy for that population.

12 years	17 years	Deferred	11/27/00

Comments: There are sufficient data to determine efficacy and safety down to and including age 12 years.

18 years	Adult	Completed	11/27/00

Comments: N/A

This page was last edited on 11/27/00

/S/ 11/27/00

Signature Date

/S/ 11/27/00

APPEARS THIS WAY
ON ORIGINAL

1.6 Item 16: Debarment Certification

In accordance with Section 306(k)(1) of the Federal Food Drug and Cosmetic Act, we hereby certify that, in connection with this NDA 50-769 for Benzamycin [redacted] (erythromycin 3% and benzoyl peroxide 5% gel), Dermik Laboratories, Inc. did not and will not use in any capacity the services of any person debarred under the Mandatory Debarment provisions [Section 306(a)] or the Permissive Debarment provisions [Section 306(b)] of the Federal Food Drug and Cosmetic Act in connection with this application.

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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Competing This Form

1. APPLICANT'S NAME AND ADDRESS
Dermik Laboratories
500 Arcola Road
Collegeville, PA 19426-0107

2. TELEPHONE NUMBER (*Include Area Code*)
(610) 454-3026

3. PRODUCT NAME
Benzamycin® (erythromycin and benzoyl peroxide)

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. YES

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

X THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

6. LICENSE NUMBER / NDA NUMBER
N050769

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 A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) 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 COMMERCIALLY (*Self Explanatory*)

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES X NO (*See reverse side if answered YES*)

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

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:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

A 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.

SIGNATURE OF AUTH	TITLE	DATE
Ronald F. Panner /S/	Senior Director Worldwide Regulatory Affairs	December 16, 1999

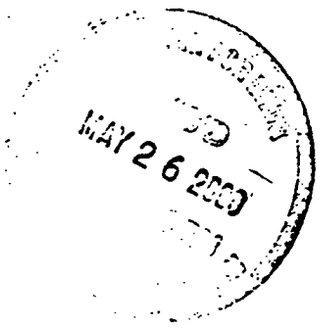
FORM FDA 3397 (5/98) Created by Electronic Document Services/USDHHS: (301) 443-2454 EF

A RHÔNE-POULENC RORER COMPANY
Dedicated to Dermatology™

500 ARCOLA ROAD
P.O. BOX 1200
COLLEGEVILLE, PA 19426-0107
TEL. 610-454-8000

NDA [illegible] AMENDMENT

May 25, 2000



Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental
Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation V
Food and Drug Administration
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

ORIGINAL

SU

NDA #50-769
Benzamycin [redacted]
(3% erythromycin and 5% benzoyl peroxide gel)

Safety Update Report

Dear Dr. Wilkin:

Our New Drug Application for Benzamycin® [redacted] is submitted to the Food and Drug Administration January 26, 2000. Therefore, the submission of a 120 day (4 month) Safety Update Report is required on or before May 26, 2000. This letter serves as a Safety Update Report for our Benzamycin [redacted] application.

Please be informed that no clinical trials have been conducted with Benzamycin [redacted] that were not included in the original NDA submission. Therefore, there is no additional clinical study safety information to provide at this time. Additionally, Dermik is not aware of any other safety information that may reasonably affect the statement of contraindications, warnings, precautions, and adverse reactions included in the draft labeling submitted in our original application.

We believe this submission fully responds to the safety update requirement. If you have any questions or require any additional information, please contact me at (610) 454-3027.

Sincerely yours,

/S/

James P. Thompson
Manager
Worldwide Regulatory Affairs

JPT/maf
Enclosures

1.9 Item 19B: Financial Disclosure

This section contains financial disclosure information for the investigators participating in the Benzamycin (erythromycin 3% and benzoyl peroxide 5% gel) clinical studies included in this submission.

All patients and subjects participating in clinical studies included in this application completed their studies before February 2, 1999. To the best of our knowledge, no investigator participating in any study included in this dossier met any of the following criteria requiring financial disclosure:

- Received any compensation such as cash, stock, royalty interest, etc... which was dependent on favorable study outcome.

- Has ownership in RPR whose value cannot be readily determined through reference to public prices. Dermik is a wholly owned subsidiary of Rhône-Poulenc Rorer which is a wholly owned subsidiary of Rhône-Poulenc, a publicly traded company. Ownership of stock in RP can, therefore, be readily determined through reference to public prices.

- Has a proprietary interest in Benzamycin (erythromycin 3% and benzoyl peroxide 5% gel) such as patent, trademark, copyright, or licensing agreement.

Public Health Service
Food and Drug Administration

Expiration Date: 3/31/02

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☐ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	See attached list	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Sharon Levy, M.D.	Director, Clinical Research
FIRM/ORGANIZATION: Dermik Laboratories	
/S/	DATE: 21 Feb 2000

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

Created by Electronic Document Services/USDHHS: (301) 443-2454 EF

Financial Disclosure for Benzamycin Dual Pouch (DL-6026) NDA (#50-769)

STUDY NO.	NAME (Principal or Subinvestigator)	DISCLOSURE OBTAINED	TYPE OF STUDY
DL-6026-9708		Yes	Phase I RIPT (Patch test)
DL-6026-9709		Yes Yes	Phase III Safety & Efficacy
DL-6026-9709		Yes Yes	Phase III Safety & Efficacy
DL-6026-9709		Yes	Phase III Safety & Efficacy
DL-6026-9709		Yes Yes	Phase III Safety & Efficacy
DL-6026-9709		Yes Yes	Phase III Safety & Efficacy
DL-6026-9709		Yes	Phase III Safety & Efficacy
DL-6026-9717	-inv) b-inv)	Yes Yes Yes Yes Yes Yes	Phase I Single-dose PK
DL-6026-9723		Yes	Phase III Safety & Efficacy
DL-6026-9723		Yes Yes	Phase III Safety & Efficacy
DL-6026-9723		Yes Yes Yes	Phase III Safety & Efficacy
DL-6026-9723		Yes Yes	Phase III Safety & Efficacy
DL-6026-9802		Yes	Phase I Use Study (non-IND)
DL-6026-9819	)	Yes Yes	Phase I Use Study

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINSTRATION	**OPDRA POSTMARKETING SAFETY REVIEW**	
TO: Jonathan K. Wilkin, M.D., Director Division of Dermatologic and Dental Drug Products HFD-540	**FROM:** Marilyn R. Pitts, Pharm.D., Safety Evaluator DDRE I (HFD- 430)	**OPDRA PID #** D000670 NOV 7 2000
DATE REQUESTED: November 7, 2000	**REQUESTOR/Phone #:** Brenda Vaughan, MD/301-827-2022	
DATE RECEIVED: October 26, 2000		
DRUG: Erythromycin Topical, Benzoyl Peroxide + Erythromycin	**NDA/IND #** 50-557, 50-769	**SPONSOR:** Dermik Labs

DRUG NAME (TRADE):
Benzamycin®

INDICATION:
BENZAMYCIN® Topical Gel is indicated for the topical treatment of acne vulgaris

EVENT:
- Pseudomembranous Colitis or Diarrhea Associated with Benzamycin®, Erythromycin Topical
- Photosensitivity or Sunburn Reactions Associated with Benzamycin® Gel

EXECUTIVE SUMMARY:

All cases of diarrhea, colitis and photosensitivity temporally associated with topical erythromycin were reviewed. There were nine US cases found, four of which were excluded for various reasons (oral erythomycin-3, report not legible-1). Two cases resulted in hospitalization, two resulted in treatment with a prescription drug, and none resulted in death. All others were considered non-serious.

There were two cases of diarrhea (1) and pseudomembranous colitis (1) temporally associated with topical erythromycin. There were no cases of Benzamycin® found, and one case each of T-Stat® and Erycette®. Neither of the two cases resulted in hospitalization. The pseudomembranous case was poorly documented and did not provide information on stool cultures, or if previous oral antibiotic therapy had been used. The patient was treated with a prescription drug and was not hospitalized. The other case reported diarrhea in a patient with previous oral tetracycline use.

There were three cases of photosensitivity temporally associated with topical erythromycin administration, with none of the cases reported with the Benzamycin® brand product. All cases were considered non-serious. Two of the cases had outcomes of "other", and one case did not report an outcome. Two of the three cases were confounded by the concomitant administration of minocycline, which is labeled for photosensitivity.

Upon review of the cases there does not appear to be a signal for pseudomembranous colitis, or photosensitivity with topical erythromycin products.

RELEVANT PRODUCT LABELING:

Warnings

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

Benzamycin® is not labeled for photosensitivity reactions.

Search Date: November 3, 2000	**Search Type (s):** X AERS ___ SRS ___ Literature ___ Other ___ *DataMart

SEARCH CRITERIA:

The AERS database was searched on November 3, 2000 for cases of pseudomembranous colitis, diarrhea, and photosensitivity temporally associated with Benzamycin®, benzagel, benzoyl peroxide + erythromycin and erythromycin administered topically, cutaneously and/or transdermally. The following search terms were used:

Colitis Haemorrhagic - (PT)
Colitis Pseudomembranous - (PT)
Colitis Ulcerative - (PT)
Diarrhea NOS - (PT)
Photosensitivity Conditions - (HLT)

SEARCH RESULTS:

There were nine unduplicated erythromycin cases found; five cases of diarrhea/colitis, and four cases of photosensitivity. There were no cases found involving the combination product Benzamycin®. The cases of diarrhea/colitis and photosensitivity will be discussed separately.

Diarrhea/Colitis

There were five cases of diarrhea and/or colitis found. Three of the five cases were excluded because erythromycin was administered orally, and not topically. One of the two remaining cases involving pseudomembranous colitis was poorly documented. The other case reported diarrhea in a patient with previous tetracycline-associated diarrhea. Both cases are described below.

FDA 4865300, MFR# 911041399, 1991 NY. A 19-year-old female reportedly developed pseudomembranous colitis, after approximately 2 months of Erycette® use. She was also on concomitant Retin A. No further information was provided.

FDA 4444899, Direct Report, 1985 NY. A 34-year-old male developed diarrhea (up to 5 loose stools daily) approximately 5 months after starting topical T-Stat®. Stool cultures obtained were negative for *Clostridium difficile*. T-Stat® was discontinued and symptoms continued for 10 days after discontinuation. The patient was not hospitalized, was treated with an unspecified prescription drug and recovered. The patient had previously experienced diarrhea with oral tetracycline use approximately 6 months prior to the current event.

Photosensitivy Reactions

There were four cases of photosensitivity reactions found. One case was excluded due to illegibility of the report. The remaining three cases were reviewed. Two of the three cases were confounded with the concomitant use of minocycline, which is labeled for phototoxicity. All three cases are described below.

FDA 3199584 MFR# 3199584 1998 Unknown. A male patient in his teens used one application of topical erythromycin 2% on his temples, cheeks and chin. The patient experienced burning and irritation. The patient then went into the sunlight, and experienced desquamation and hyperpigmentation the following day. With topical corticosteriod use, the desquamation and hyperpigmentation cleared in 5 to 7 days. The patient had been concomitantly receiving minocycline and benzoyl peroxide, which he continued to use. The topical erythromycin was discontinued.

FDA 4478668 MFR# ERY-1 1985 MA A female of unknown age spent 6 hours in the summer sun and experienced facial blisters while using Erycette®. There were no concomitant medications reported.

FDA 5453870 MFR# 1995 Unknown. A 28-year-old male concomitantly receiving Erycette® and Retin A developed a rash with little white pimples on the chin, either side of the lips, and in the moustache area when he went out into the sun. Additionally, he had been using minocycline and Purpose soap for eight months. The patient prophylactically used a sunscreen prior to sun exposure but still developed the little white bumps. The patient was reported as not recovering from the reaction at the time of the report.

DISCUSSION / CONCLUSIONS:

There were two cases of diarrhea (1) and pseudomembranous colitis (1) temporally associated with topical erythromycin. Neither of the cases involved the use of Benzamycin®. One was reported with Erycette® and the other was reported with T-Stat®. The pseudomembranous case was poorly documented and did not provide information on stool cultures, or if previous oral antibiotic therapy had been used. The patient was treated with a prescription drug and was not hospitalized.

There were three cases of photosensitivity temporally associated with topical erythromycin. None of the cases involved the use of Benzamycin®. Two were reported with Erycette® and the third with 2% topical erythromycin. Two cases were confounded by the concomitant administration of minocycline, a tetracycline labeled for phototoxic events. The remaining case was poorly documented.

Upon review of the cases there does not appear to be a signal for pseudomembranous colitis, or photosensitivity with Benzamycin® or other topical erythromycin products.

Medical Officer / Safety Evaluator / Date: /S/ Nov 1 2000	Team Leader's Signature / Date: /S/ 11/6/00
Division Director Signature / Date: /S/ 11-7-00	Office Director Signature / Date:

cc: NDA # 50-557, 50-769
HFD-540/Vaughan/Cross
HFD-430/Beitz/Trontell/Karwoski/Guinn
HFD-400/Honig
Electronic File Name: Benzamycin and Diarrhea II

APPEARS THIS WAY
ON ORIGINAL

20 Pages have been redacted in full from this document

Reason:

_____ b(2) 'low'
_____ b(4) CCI
__X__ b(4) TS SPECIFICATIONS AND TESTS
_____ b(5) Deliberative Process: Attorney Client and Attorney Work Product Privilege
_____ b(6) Personal Privacy
_____ b(7) Law Enforcement Records

Electronic Mail Message

Date: 4/4/00 7:42:15 AM
From: Jerry Phillips (PHILLIPSJ)
To: Frank Cross, Jr. (CROSSF)
Cc: Sammie Beam (BEAMS)
Cc: Peter Honig (HONIGP)
Subject: OPDRA Consult 00-098; Benzamycin

Frank:

This is an official response to a 3/20/00 consult from HFD-540 for a tradename consult for Benzamycin ——— The proposed name Benzamycin is already approved proprietary name and this represents a new unit-of-use packaging (0.8 g) configuration in which Benzoyl Peroxide and Erythromycin are in pouches.

OPDRA has no objection to the use of the proprietary name 'Benzamycin

We have also reviewed the labeling and have no comments to offer.

If you have any questions you can feel free to call me (7-3246) or Sammie Beam (7-3161). Thanks.

y

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ON ORIGINAL

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

DATE RECEIVED: 8/8/2000	DUE DATE: 10/27/2000	OPDRA CONSULT #: 00-0220

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

THROUGH:
Frank Cross
Project Manager
HFD-540

PRODUCT NAME:	MANUFACTURER: Dermik Laboratories, Inc.
Benzamycin Pak (Erythromycin 3%-Benzoyl Peroxide 5% Topical Gel) NDA #: 50-769	

SAFETY EVALUATOR: Peter Tam, RPh.

OPDRA RECOMMENDATION:
OPDRA has no objections to the use of the proprietary name, Benzamycin Pak.

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

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

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

/S/ 10/24/2000

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

/S/ 10/24/00

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

Office of Post-Marketing Drug Risk Assessment
HFD-400; Rm. 15B03
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: 10/13/2000

NDA#: 50-769

NAME OF DRUG: Benzamycin Pak
(Erythromycin 3%-Benzoyl Peroxide 5% Topical Gel)

NDA HOLDER: Dermik Laboratories, Inc.

I. INTRODUCTION:

This consult is written in response to a request from the Division of Dermatologic and Dental Drug Products, (HFD-540) received on 8/8/2000 to review the proposed proprietary name, Benzamycin Pak.

The sponsor previously submitted the proposed name, ——— wanted to change the modifier from ——— to a new modifier "Pak", and requested review by OPDRA. The new goal date is 10/27/2000.

PRODUCT INFORMATION

Each Benzamycin Pak pouch contains 0.8 grams of product which, as dispensed, consists of 3% erythromycin and 5% of benzoyl peroxide. Each of these ingredients is contained in a separate chamber within the pouch. At the time of use, the patient is instructed to empty the entire contents (two gels, one clear and one white) into a small area of the palm. Carefully blend the two gels with fingertip and apply immediately to the affected area.

Benzamycin Pak is indicated for the topical treatment of acne vulgaris. It should be applied twice daily, morning and evening to affected areas after the skin is thoroughly washed, rinsed with warm water and gently patted dry.

Benzamycin Pak will be supplied in boxes of 60 pouches.

In addition, Dermik Laboratories also currently market Benzamycin Topical Gel containing two vials in a kit. Before dispensing, the pharmacist has to mix the erythromycin powder with 3 ml ethyl alcohol and benzoyl peroxide powder (in a separate vial) to form a gel. After reconstitution, the final preparation contains 23.3 gm of Benzamycin Topical Gel.

II. RISK ASSESSMENT:

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

A. EXPERT PANEL DISCUSSION

An Expert Panel Discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name, Benzamycin Pak. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA's Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. There were no proprietary names for currently marketed U.S. products identified by the Expert Panel that were believed to have significant look-alike and sound-alike properties. However, there are many existing products that have a similar modifier "Pak" or "Pack" associated with the product names. Examples are 1) Monistat Dual-Pak (Rx only), 2) Mycelex Twin Pack (Rx only), 3) Gyne-Lotrimin Combination Pack (OTC), and 4) Monistat 7 Combination Pack (OTC).

2. DDMAC – no objection.

[1] MICROMEDEX Healthcare Intranet Series, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Emergindex, Reprodisk, Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc).

[2] American Drug Index, online version, Facts and Comparisons, St. Louis, MO.

[3] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

[4] Drug Product Reference File [DPR], the Established Evaluation System [EES], the AMF Decision Support System [DSS], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

[5] WWW location http://www.uspto.gov/tmdb/index.html.

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Studies were conducted by OPDRA and involved 90 health professionals comprised of pharmacists, physicians, and nurses within FDA to determine the degree of confusion of Benzamycin Pak with other drug names due to the similarity in handwriting and verbal pronunciation of the name. Inpatient and outpatient prescriptions were written, each consisting of known drug products and a prescription for Benzamycin Pak (see below). These prescriptions were scanned into a computer and were then delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Benzamycin Pak 1 box Sig: Used as directed	Outpatient: Benzamycin Pak 1 box , Use as directed
Inpatient RX: Benzamycin Pak used as directed 1 box	

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Outpatient	31	18(58%)	13	5
Verbal	29	15(52%)	9	6
Written Inpatient	30	13(43%)	6	7
Total	90	46(51%)	28(61%)	18(39%)

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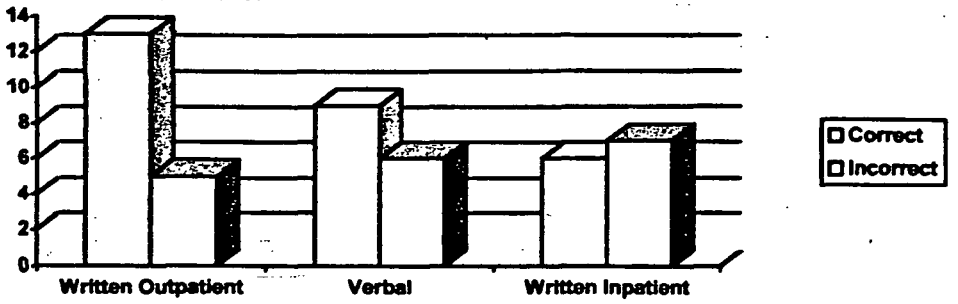


Thirty-nine percent of participants responded with the incorrect name. The incorrect written and verbal responses are summarized in Table II.

Table II

Written Outpatient	Incorrectly Interpreted
	Benzamycin (5)
Verbal	Benzomycin
	Benzamycin (5)
Written Inpatient	Benzamycin (5)
	Benzamycin 1 box
	Benzamycin Dak

The results of the verbal prescription study indicate that nine out of fifteen respondents interpreted Benzamycin Pak incorrectly. In the first written study, five out of eighteen respondents interpreted Benzamycin Pak incorrectly. In the second written (inpatient) study, seven out of thirteen respondents interpreted Benzamycin Pak incorrectly. This might be due to a poorly written script in the second written study. In addition, a total of 15 respondents interpreted Benzamycin Pak as Benzamycin. The other incorrect responses were mostly misspelled/phonetic variations of the proposed drug name. The incorrect interpretations in all three studies of the proposed name did not overlap with any existing product.

C. SAFETY EVALUATOR RISK ASSESSMENT

The Expert Panel did not identify any proprietary names for currently marketed U.S. products that were believed to have significant sound-alike and look-alike qualities relative to Benzamycin Pak.

In the prescription studies, 39% of the participants responded with an incorrect name. None of these names overlapped with any existing products. However, 15 respondents omitted the modifier "Pak" in their name interpretation.

There is some potential confusion regarding the exact quantity to be dispensed for a Benzamycin Pak prescription. If, for example, a prescription is written for Benzamycin gel #1, two possibilities for the quantity dispensed exist:

1. Benzamycin Topical Gel 23.3 gm (consists of two vials in a kit) could be dispensed.
2. A box of Benzamycin Pak consists of 60 pouches (0.8gm each) could also be dispensed.

Since Benzamycin Pak and Benzamycin Topical Gel have identical formulation, dosage form,

same ingredients (3% erythromycin and 5% benzoyl peroxide), dosing interval, and indication, these two products can be used interchangeably with similar patient outcome. Aside from the potential confusion on the exact quantity dispensed, medication error due to the name confusion between these products appears unlikely.

In fact, from a medication error perspective, we have no significant concern. For these reasons, we do not object to the proposed name, Benzamycin Pak.

III. RECOMMENDATIONS:

OPDRA has no objections to the use of the proprietary name, Benzamycin Pak.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Peter Tam at 301-827-3241.

/S/ 6/00

Peter Tam, R.Ph.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

/S/ 10/24/2000

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

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-769

FEB 4 2000

Dermik Labs, Inc.
Attention: Ronald F. Panner
Director, Worldwide Regulatory Affairs
500 Arcola Avenue
PO Box 5096
Collegeville, PA 19426

Dear Mr. Panner:

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: [redacted]

Therapeutic Classification: Standard (S)

Date of Application: January 26, 2000

Date of Receipt: January 27, 2000

Our Reference Number: NDA 50-769

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on March 27, 2000 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be November 27, 2000 and the secondary user fee goal date will be January 27, 2001.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products, HFD-540
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products, HFD-540
9201 Corporate Blvd.
Rockville, Maryland 20850-3202

APPEARS THIS WAY
ON ORIGINAL

If you have any questions, call Frank H. Cross, Jr., Project Manager, at (301) 827-2020.

Sincerely,

/S/ 2/2/00

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

cc:
Archival NDA 50-769
HFD-540/Div. Files
HFD-540/F.H.Cross
HFD-540/S. Walker
HFD-540/M.Okun
HFD-540/W.DeCamp
HFD-540/A.Jacobs
DISTRICT OFFICE
Drafted by: smc/February 1, 2000
filename: N50769.ACK

ACKNOWLEDGEMENT (AC)

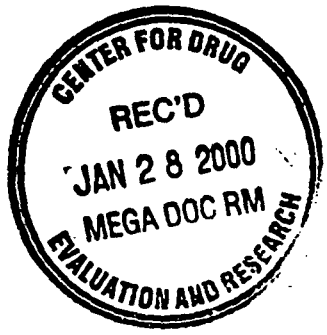
APPEARS THIS WAY
ON ORIGINAL

DERMIK LABORATORIES, INC.
A RHÔNE-POULENC RORER COMPANY
Dedicated to Dermatology™

500 ARCOLA ROAD
P.O. BOX 1200
COLLEGEVILLE, PA 19426-0107
TEL. 610-454-8000

January 26, 2000

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and
Dental Drug Products
Attention: Document Control Room
Food and Drug Administration
Park Building, Room 214
12420 Parklawn Drive
Rockville, MD 20852



New Drug Application No. 50-769

(erythromycin 3% and benozyl peroxide 5% gel)

ORIGINAL NEW DRUG APPLICATION

Dear Dr. Wilkin:

In accordance with 21 CFR 314.50 of the Federal Food, Drug and Cosmetic Act, Dermik Laboratories, Inc. is submitting an original New Drug Application for _____ (erythromycin 3% and benzoyl peroxide 5% gel) which demonstrates the efficacy and safety of the product in the topical treatment of patients with acne vulgaris.

This application contains the following sections: 1) Index, 2) Draft Labeling, 3) Application Summary, 4A) Chemistry, Manufacturing and Controls, 4B) Sample Information, 4C) Methods Validation Package, 5) Nonclinical Pharmacology and Toxicology, 6) Human Pharmacokinetics and Bioavailability, 7) Microbiology, 8) Clinical Data, 10) Statistical, 11) Case Report Tabulations, 12) Case Report Forms, 13) Patent Information, 14) Patent Certification, 16) Debarment Certification, 17) Field Copy Certification, 18) User Fee Cover Sheet, 19A) Pediatric Use, and 19B) Financial Disclosure.

Case Report form tabulations for the individual medical reports and case report forms for patients that discontinued a study after experiencing an adverse event are included in the appendices of each report which are located in Items 8 Clinical and 10 Statistical of this application. These documents are also included in Items 11 Case Report Tabulations and 12 Case Report Forms.

Some information in this application is included in electronic format consisting of SAS datasets for the pivotal clinical trials. Also included are electronic copies of final study reports for the phase III trials and the integrated summaries. This information is contained on diskettes that are attached in a pocketed plastic sleeve located after the last page in volume 1. No computer viruses were detected when these disks were scanned using Doctor Solomon's Software, LTD Version 7.99.

In accordance with the Prescription Drug Use Fee Act of 1992, a check No. 708570, in the amount of $272,282.00 was sent to the Food and Drug Administration, Pittsburgh, Pennsylvania on December 16, 1999. This application was assigned User Fee Identification Number 3882.

As required by Section 306(k)(1) of the Generic Drug Enforcement Act {21 U.S.C. 335a (k)(1)}, we hereby certify that, in connection with this application, Dermik Laboratories, Inc. did not and will not use in any capacity the services of any person debarred under subsections 3-6(a) or (b) of the act.

Dermik Laboratories, Inc. considers the information in this application to be confidential and proprietary and we request that no portions thereof be disclosed to third parties, under FOI or otherwise, without first obtaining written consent from Dermik Laboratories, Inc.

If you have any questions or require any additional information during review of this application, please contact me at (610) 454-3026.

Sincerely,

/S/

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

Field Copy:

Debra L. Pagano
Philadelphia District Pre-Approval Manager
U.S. Food and Drug Administration
Room 900, U.S. Customhouse
2nd and Chestnut Streets
Philadelphia, PA 19106-2973

APPEARS THIS WAY
ON ORIGINAL

DERMIK LABORATORIES, INC.
A RHONE-POULENC RORER COMPANY
Dedicated to Dermatology

500 ARCOLA ROAD
P.O. BOX 1200
COLLEGEVILLE, PA 19426-0107
TEL. 610-454-8000

February 21, 2000

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental
Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation V
Food and Drug Administration
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

NDA #50-769

(3% erythromycin and 5% benzyl peroxide gel)

Response to FDA Request for Information

Dear Dr. Wilkin:

Reference is made to February 7 and February 16, 2000 telephone calls Dermik received from Commander Frank Cross, Jr. requesting the submission of additional information concerning the Benzamycin NDA.

Included in this submission are Dermik's responses to Commander Cross' requests.

If you have any questions or require any additional information, please contact me at (610) 454-3027.

Sincerely yours,

James P. Thompson
Manager
Worldwide Regulatory Affairs

JPT/arz
Enclosures

ORIGINAL

DERMIK LABORATORIES, INC.
Dedicated to Dermatology
A RHÔNE-POULENC RORER COMPANY

500 ARCOLA ROAD
P.O. BOX 1200
COLLEGEVILLE, PA 19426-0107
TEL. 610-454-8000

March 22, 2000

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental
Drug Products
Center for Drug Evaluation and Research
Office of Drug Evaluation V
Food and Drug Administration
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

NC

NDA #50-769
Benzamycin®
(3% erythromycin and 5% benzyl peroxide gel)

Response to FDA Request for Information

Dear Dr. Wilkin:

Reference is made to a March 21, 2000 telephone conversation I had with Senior Regulatory Management Officer Commander Frank H. Cross Jr. concerning financial disclosure forms that were not included in the NDA for three investigators, Morris Shelanski, M.D., Joseph Shelanski and Robert Donovan, M.D. Commander Cross requested the submission of copies of these financial disclosure forms.

Included in this submission is the requested information. Please be informed that all of the clinical studies submitted to the Benzamycin® NDA, including the studies conducted by were completed before February 2, 1999, the effective date of the regulations concerning the disclosure of financial interests and arrangements of clinical investigators.

If you have any questions or require any additional information, please contact me at (610) 454-3027.

Sincerely yours,

James P. Thompson

James P. Thompson
Manager
Worldwide Regulatory Affairs

JPT.lg
Enclosures

DUPLICATE

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
NDA 50-769

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAR 24 2000
MEGA

APPLICATION INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Dermik Laboratories, Inc.	March 23 2000
TELEPHONE NO. (*Include Area Code*)	FACSIMILE (FAX) Number (*Include Area Code*)
(610) 454-3027	(610) 454-5287
APPLICANT ADDRESS (*Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued*):	AUTHORIZED U.S. AGENT NAME & ADDRESS (*ZIP Code, telephone & FAX number*) IF APPLICABLE
500 Arcola Road P.O. Box 5096 Collegeville, PA 19426	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) NDA 20-985

ESTABLISHED NAME (*e.g., Proper name, USP/USAN name*)	PROPRIETARY NAME (*trade name*) IF ANY
(erythromycin and benzoyl peroxide)	Benzamycin®

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (*If any*)	CODE NAME (*If any*)
See Original Application	DL-6026

DOSAGE FORM:	STRENGTHS	ROUTE OF ADMINISTRATION:
topical gel	erythromycin 3% and benzoyl peroxide 5%	topical

(PROPOSED) INDICATION(S) FOR USE: Topical treatment of acne vulgaris

APPLICATION INFORMATION

APPLICATION TPE
(check one) X 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 X 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 — Holder of Approved Application

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

REASON FOR SUBMISSION FDA Request for additional information.

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

NUMBER OF VOLUMES SUBMITTED n/a

THIS APPLICATION IS x 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 Original Application

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

See Original Application