CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-985

ADMINISTRATIVE DOCUMENTS

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 20-995 Drug Tovipersone 5-Fluorouracil cream, 5% Applicant Dermik Laboratories, Inc

RPM Victoria Lukasak Phone 301-827-2073

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

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

Pivotal IND(s) IND _____

Application classifications:
Chem Class Antimetabolite/cytotoxic
Other (e.g., orphan, OTC) _____

PDUFA Goal Dates:
Primary 8/26/00
Secondary 10/27/00

Arrange package in the following order:

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

GENERAL INFORMATION:

- User Fee Information: ☑ User Fee Paid
  ☐ User Fee Waiver (attach waiver notification letter)
  ☐ User Fee Exemption
- Action Letter..... ☑ AP ☐ AE ☐ NA
- Labeling & Labels
  FDA revised labeling and reviews..... ✓
  Original proposed labeling (package insert, patient package insert) ..... ✓
  Other labeling in class (most recent 3) or class labeling.....
  Has DDMAC reviewed the labeling? ..... ☑ Yes (include review) ☐ No
  Immediate container and carton labels .....
  Nomenclature review ..... ✓
- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is ☑ is not on the AIP.
  Exception for review (Center Director's memo).....
  OC Clearance for approval.....

Continued ⇨ 1

- Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review) ☐ Materials requested in AP letter
- Post-marketing Commitments
  - Agency request for Phase 4 Commitments ..... ✓
  - Copy of Applicant's commitments ..... ✓
- Was Press Office notified of action (for approval action only)? ..... ☐ Yes ☐ No
  - Copy of Press Release or Talk Paper .....
- Patent
  - Information [505(b)(1)] ..... ✓
  - Patent Certification [505(b)(2)] .....
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)] .....
- Exclusivity Summary ..... ✓
- Debarment Statement ..... ✓
- Financial Disclosure
  - No disclosable information ..... ✓
  - Disclosable information – indicate where review is located .....
- Correspondence/Memoranda/Faxes ..... ✓
- Minutes of Meetings .....
  - Date of EOP2 Meeting _____
  - Date of pre NDA Meeting 7-26-1991
  - Date of pre-AP Safety Conference _____
- Advisory Committee Meeting ..... NA
  - Date of Meeting .....
  - Questions considered by the committee .....
  - Minutes or 48-hour alert or pertinent section of transcript .....
- Federal Register Notices, DESI documents ..... NA

CLINICAL INFORMATION:

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

- Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) ..... ø
- Clinical review(s) and memoranda ..... ✓

Continued ⇨2

- Safety Update review(s) ..... Ø
- Pediatric Information
  ☑ Waiver/partial waiver (Indicate location of rationale for waiver) ☐ Deferred ✓
  Pediatric Page ..... _____
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☒ Not Applicable
- Statistical review(s) and memoranda ..... ✓
- Biopharmaceutical review(s) and memoranda ..... ✓
- Abuse Liability review(s) ..... Ø
  Recommendation for scheduling ..... Ø
- Microbiology (efficacy) review(s) and memoranda ..... Ø
- DSI Audits ..... ✓
  ☑ Clinical studies ☐ bioequivalence studies ..... _____

CMC INFORMATION:

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

- CMC review(s) and memoranda ..... ✓
- Statistics review(s) and memoranda regarding dissolution and/or stability ..... _____
- DMF review(s) ..... ✓
- Environmental Assessment review/FONSI/Categorical exemption ..... ✓
- Micro (validation of sterilization) review(s) and memoranda ..... ✓
- Facilities Inspection (include EES report)
  Date completed 7-11-2000 ..... ☑ Acceptable ☐ Not Acceptable
- Methods Validation ..... ☐ Completed ☑ Not Completed

PRECLINICAL PHARM/TOX INFORMATION:

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

- Pharm/Tox review(s) and memoranda ..... ✓
- Memo from DSI regarding GLP inspection (if any) ..... Ø

Continued ⇨3

- Statistical review(s) of carcinogenicity studies ..... Ø
- CAC/ECAC report ..... Ø

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
Cream 0.5% (fluorouracil cream)

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
3825

6. LICENSE NUMBER / NDA NUMBER
N020985

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) 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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Ronald F. Panner	Senior Director Worldwide Regulatory Affairs	October 12, 1999

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 20-985 for [redacted] Cream 0.5% (fluorouracil cream), 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.

APPEARS THIS WAY
ON ORIGINAL

FINANCIAL DISCLOSURE

Dermik 5-FU 0.5% Cream (DL6025)

This section contains financial disclosure information for the investigators participating in the two pivotal efficacy and safety studies included in this submission (DL6025-9721 and 9722).

All patients reported on in this dossier completed study 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 5-fluorouracil 0.5% cream such as patent, trademark, copyright or licensing agreement.

APPEARS THIS WAY
ON ORIGINAL

PHONE-POULENC

Rhône-Poulenc Rorer

ATTACHMENT C

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: 3/31/02

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 SHARON LEVY, M.D.	TITLE DIRECTOR OF CLINICAL RESEARCH
FIRM/ORGANIZATION DERMIK LABORATORIES, INC.	
SIGNATURE [signature]	DATE OCT 7, 1999

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

FORM FDA 3454 (3/99)

Created by Electronic Document Services/USDHHS: (301) 443-3464 EF

WITHHOLD 2 PAGE (S)

Item 13 -Patent/Exclusivity Information

1)	Active Ingredient(s):	5-fluorouracil
2)	Strength(s):	0.5%
3)	Trademark:	
4)	Dosage Form (Route of Administration):	Topical cream
5)	Application Firm Name:	Dermik Laboratories, Inc.
6)	IND Number:	
7)	NDA Number:	20-985
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:	4,690,825, expiration October 4, 2005

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	4,690,825
2)	Date of expiration	October 4, 2005
3)	Type of patent	drug product (formulation/composition); method of use
4)	Name of patent owner	Advanced Polymer Systems, Inc.
5)	U.S. representative	Dermik Laboratories, Inc.

The undersigned declares that Patent No. 4,690,825 covers the formulation, composition, and/or method of use of Applicant's ——5-fluorouracil) product. This product is the subject of this application for which approval is being sought.

Signed: _____ Date: 10/18/99

Name: Ross J. Oehler

Title: Assistant General Counsel,
Director, U.S. Patent and Trademark Dept.
Rhône-Poulenc Rorer Pharmaceuticals Inc.

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY FOR NDA 20-985

Trade Name No Tradename

Generic Name 5-FLUOROURACIL Cream, 0.5%

Applicant Name Dermik Laboratories, Inc. HFD # 540

Approval Date If Known October 27, 2000

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 /✓/ NO /__/

b) Is it an effectiveness supplement?

YES /__/ NO /✓/

If yes, what type? (SE1, SE2, etc.) NA

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 /✓/ 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.

NA

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:

NA

d) Did the applicant request exclusivity?

YES /✓/ NO /__/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years years

e) Has pediatric exclusivity been granted for this Active Moiety?

Yes/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 /__/ NO /✓/

If yes, NDA #_____. Drug Name _____.

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 /✓/

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 /__/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 16-831 EFUDEX
NDA# 16-982 Fluoroplex 1%
NDA# 12-204 Fluorouracil

NDA 16-765 Fluoroplex 1%

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 /___/ NO /✓/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

[redacted]

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 /✓/ 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 /✓/ 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 /✓/ 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 /✓/

(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 /✓/

(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: over —

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 YES /__/ NO /✓/

Investigation #2 YES /__/ NO /✓/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

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 YES /__/ NO /✓/

Investigation #2 YES /__/ NO /✓/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

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"): Study DL 6025-9721

Study DL 6025-9722

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 #1

IND ——— YES /✓/ NO /__/ Explain: _____

Investigation #2

IND _____ YES /✓/ NO /___/ Explain: _____

(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? N/A

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

(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 /✓/

/S/ Oct. 19, 2000

Signature Date

Title: Project Manager

/S/ 10/27/00

Signature of Division Director Date

cc: Original NDA Division File HFD-93 Mary Ann Holovac

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA/PLA/PMA # 20-985 Supplement # 0 Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-540 Trade and generic names/dosage form: Actinic Keratosis (5-fluorouracil) cream, 0.5% Action: AP AE NA

Applicant Dermik Laboratories, Inc Therapeutic Class antimetabolite/cytotoxic

Indication(s) previously approved None

Pediatric information in labeling of approved indication(s) is adequate ✓ inadequate ___

Proposed indication in this application For the topical treatment of multiple actinic or solar keratosis of the face and scalp

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? ___ Yes (Continue with questions) ___ No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

___Neonates (Birth-1month) ___Infants (1month-2yrs) ___Children (2-12yrs) ___Adolescents(12-16yrs)

___ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

___ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

___ 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

- ___ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.
- ___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.
- ___ c. The applicant has committed to doing such studies as will be required.
  - ___ (1) Studies are ongoing,
  - ___ (2) Protocols were submitted and approved.
  - ___ (3) Protocols were submitted and are under review.
  - ___ (4) If no protocol has been submitted, attach memo describing status of discussions.
- ___ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

✓ 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed. See Back

___ 5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? ___ Yes ✓ No

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from the medical review of NDA 20-985, mo. Brenda Vaughan, M.D., Martin Okun, M.D. (e.g., medical review, medical officer, team leader).

/S/

Project Manager

Signature of Preparer and Title

Oct. 19, 2000

[/S/ 10/27/00]

cc: Archival NDA/PLA/PMA # 20-985
HFD-540 /Div File
NDA/PLA Action Package
HFD-104/Peds/T.Crescenzi

(revised 3/6/00)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, TERRIE CRESCENZI, HFD-104 (CRESCENZIT)

In accordance with 21 CFR§314.55(c), Dermik Laboratories, Inc. hereby requests a full waiver of the requirements of 314.55 paragraph (a) because Efudex Cream 0.5% (fluorouracil cream) is not likely to be used in a substantial number of pediatric patients for the topical treatment of multiple actinic or solar keratosis of the face and scalp.

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

DATE RECEIVED: 1/7/00	DUE DATE: 3/30/00	OPDRA CONSULT #: 00-0016

TO :

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

THROUGH: Vickey Lutwak, Project Manager, DDDDP
HFD-540

PRODUCT NAME:	MANUFACTURER: Dermik Laboratories, Inc.
(fluorouracil cream) 0.5% NDA #: 20-985	
Safety Evaluator: Peter Tam, RPh.	

OPDRA RECOMMENDATION:

OPDRA does not recommend the use of the proprietary name ———

/S/ 4/3/2000

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

/S/ 4/3/00

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

cc:
Okun
Vaughan
DeCamp
Hathaway

APPEARS THIS WAY
ON ORIGINAL

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

PROPRIETARY NAME REVIEW

Date of Review: 3/21/00

NDA#: 20-985

Name of Drug: ——— (fluorouracil cream) 0.5%

NDA Holder: Dermik Laboratories, Inc.

I. INTRODUCTION

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540) on January 7th, 2000, to review the proposed proprietary drug name, ——— in regard to potential name confusion with existing proprietary/generic drug names.

PRODUCT INFORMATION

——— cream 0.5% contains 5-fluorouracil, an antineoplastic, antimetabolite product for dermatologic use. It is indicated for the topical treatment of multiple actinic or solar keratoses of the face and scalp.

There is evidence that the metabolism of fluorouracil in anabolic pathway blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this manner, fluorouracil interferes with the synthesis of deoxyribonucleic acid (DNA) and to lesser extent inhibits the formation of ribonucleic acid (RNA). Since DNA and RNA are essential for cell division and growth, the effect of fluorouracil may be to create a thymine deficiency that provokes unbalanced growth and death of the cell. The effects of DNA and RNA deprivation are most marked on those cells which grow more rapidly and take up fluorouracil at a more rapid rate.

Overall, once daily ——— is indictated for the treatment of actinic keratoses or solar keratoses of the face and scalp with at least one week of treatment. Continued treatment for 2 to 4 weeks resulted in further lesion reduction and clearing.

——— cream will be supplied in ——— 30 gm tubes.

II. RISK ASSESSMENT

In order to determine the potential for medication errors and to find out the degree of confusion of the proposed proprietary name, ———with other drug names, the medication error staff of OPDRA searched Micromedex online, PDR (1999 edition), American Drug Index (43rd Edition), Drug Facts and Comparison (update monthly), USP Drug Information (1999 edition), the Electronic Orange Book, and US Patent and Trademark Office online database. In addition, OPDRA also searched several FDA databases for potential sound-alike and look-alike names to approved /unapproved drug products through DPR (Drug Products Reference), Medline, Decision Support System (DSS), Establishment Evaluation System, and LNC database.

A. EXPERT PANEL DISCUSSION:

The expert panel consists of members of the OPDRA medication error safety evaluator staff and a representative from the Division of Drug Marketing, Advertising and Communication.

The panel discussion was conducted on 2/14/00. There is currently an OTC sunscreen on the market with an identical root name: ——— In addition, Folex, an injection with the established name, methotrexate, was thought to sound-alike to ———. The panel also objected to "———" in the proposed proprietary name ———

The panel recommended that no prescription studies be undertaken and further recommended rejecting this proposed proprietary name.

B. SAFETY EVALUATION:

The searches conducted within FDA did reveal an identical proprietary name for a different active ingredient called, ——— — sunscreen lotion, which is manufactured by —— Pharmaceuticals. ——— is listed in American Drug Index (1999 edition) as well as in USP Drug Information (1999 edition).

A potential safety risk exists, since pharmacists frequently consult these reference books for drug information. For instance, in an outpatient setting, a prescription called for ———and the dispensing pharmacist is not familiar with such an order, he/she might consult American Drug Index or

USP Drug Information if ADI is not normally available in an outpatient setting such as in a community pharmacy) and find that ——— is listed in either reference book. Thus, a patient might be referred to the OTC shelve for sunscreen ——— while the physician actually wanted ——— cream. Hence, the risk is high for an error to occur when there is an identical name for two different products.

Finally, we have some concerns about the sound-alike confusion between ——— and Folex, an antineoplastic drug which comes as an injection in 2 ml, 4 ml, and 8 ml. They both have the ——— and Folex ———". Hence, the potential safety risk due to sound-alike similarity of these two names is very high on verbal orders.

C. CONTAINER LABEL, CARTON AND INSERT LABELING:

General Comments:

1. The word "cream" is duplicated on the label and it should be deleted.

2. The term "once-a-day" should be moved to a side panel and included in the " usual dosage" statement, as required in the regulations under 201.5(c), frequency of administration or application.

3. The logo looks like a — and is distracting. The — logo probably emphasizes on solar keratoses treatment while it is also indicated for actinic keratoses. We would recommend against the use and placement of this logo with the proprietary name.

4. The term ' — ' in the trade name is overemphasized in a special bold print. We would recommend that it not be bold.

III. RECOMMENDATIONS

1. OPDRA does not recommend the use of the proprietary name ———.

2. OPDRA recommends the above labeling revisions to encourage the safest possible use of this product.

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion. Should you have any questions concerning this review, please contact Peter Tam at 301-827-3241.

/S/ 3/28/00

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

Concur

/S/ 4/3/2000

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

APPEARS THIS WAY
ON ORIGINAL

C.C.

NDA 20-985
Office File
HFD-540; Vickey Lutwak, Project Manager, DDDDP
HFD-540; Jonathan Wilkin, M.D., Division Director, DDDDP
HFD-430; Marilyn Pitts, Safety Evaluator, DDRE I
HFD-040; Mark Askine, Senior Regulatory Review Officer, DDMAC
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Honig, Director, OPDRA (electronic copy)
HFD-002; Murray Lumpkin, Deputy Center Director for Review Management
(electronic copy)

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
OPDRA-Request /Tradename 2nd request	HFD-540 Vickey Lutwak

	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
3/2000		20-895	Appeal	6-21-00

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Cream Formerly	PDUFA due date 10/28/00	antimetabolite/cytotoxic	ASAP

NAME OF FIRM: Dermik Laboratories 2.5% fluorouracil

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG EXPERIENCE

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

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

This is an appeal from the sponsor to OPDRA's decision to turn down the tradename.
Please note that the sponsor has removed ___ from the old name, and it is now just ___

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
V Lutwak, PM, HFD 540 7-2073	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

June 21, 2000

NEW CORRESP

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental
Drug Products (HFD-540)
Center for Drug Evaluation and Research
Office of Drug Evaluation V
Attention: Document Control Room
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

NC

NDA #20-985
——— Cream
(fluorouracil cream) 0.5%

General Correspondence
———Trade Name

Dear Dr. Wilkin,

Reference is made to April 6 and 11, 2000 telephone conversations I had with the DDDDP Project Manager, Ms. Victoria Lutwak, during which Dermik was told that the name ———, which Dermik Laboratories, Inc. had proposed for our fluorouracil cream product, was rejected by a FDA risk assessment committee. The primary reason given was a direct conflict of Dermik's proposed trade name with an existing drug product named ——— Another reason for the rejection was a "sound alike" conflict with a product named FOLEX.

During the same April 6, 2000 telephone conversation, Ms. Lutwak also informed Dermik that FDA had rejected the use of ——— as a modifier of Dermik's proposed trade name for our topical fluorouracil product.

Based on information included in this submission, Dermik is requesting FDA reconsideration of ———as the proprietary name for fluorouracil cream. We ask that this reconsideration be independent of the trade name modifier, ———.

BEST POSSIBLE COPY

DUPLICATE

After being told that FDA had rejected ——— as the trade name for our fluorouracil cream product, Dermik employed ' ——— , a specialist in researching and developing pharmaceutical and biologic brand names, to conduct marketing research with a significant sample of medical and pharmacy practitioners. The objective of this research was to identify any potential confusion issues in the prescribing chain that might result in patient harm. Results of the ——— study are included in the attached study report. Summary results of ——— study, that utilized 100 participating practitioners, follow:

III-Phase 2 (pg. 8)
VERBAL PRESCRIPTION RX FILLING - UNAIDED

- Pharmacists' verbatim unaided interpretation of physicians' verbal prescriptions resulted in insignificant confusion with currently marketed brand and generic name drugs. FOLEX was identified by only one (1) participating practitioner in this measurement. ——— was not identified.

III-Phase 2 (pg. 10)
SCRIPTED PRESCRIPTION RX FILLING - UNAIDED

- Pharmacists' verbatim unaided interpretation of physicians' written prescriptions resulted in no confusion with currently marketed brand and generic name drugs. No participating practitioners identified FOLEX or ———

III-Phase 3 (pg. 12-13)
SOUND-ALIKE AND LOOK-ALIKE POTENTIAL CONFUSION

- Unaided responses from both physicians and pharmacists indicated insignificant "Sound-Alike" or "Look-Alike" potential confusion with currently marketed drugs. No participating practitioners identified FOLEX or ———

IV (pg. 21-23)
COMPREHENSIVE SAFETY REVIEW

- The comprehensive safety evaluation revealed an insignificant number of marketed brand name citations, with no potential for patient harm. No participating practitioners identified FOLEX or ———

V (pg. 24-26)
POSITIVE AND NEGATIVE CONTROLS ACCURACY REVIEW

- An evaluation of Dermik's proposed proprietary brand name, ——— by pharmacists for dispensing accuracy resulted in 96% overall accuracy.

VI (pg. 27)
PHARMACISTS' EVALUATION - [redacted]

- No potential for confusion or patient harm exists, as the Pharmacia & Upjohn (FOLEX) and [redacted] products are no longer available.

The attached report reviews these conclusions in detail and describes the methodology relied upon by [redacted] Patient safety is of paramount importance to Dermik, and we are confident that the attached research shows [redacted] to be an appropriate trade name for fluorouracil cream.

In addition to conducting a marketing research study, [redacted] also investigated the current trade name status of both [redacted] and FOLEX. The results of this investigation are also included in the attached report.

[redacted] determined that [redacted] was the trade name of an OTC sunscreen, [redacted] owned by [redacted] has also determined that the [redacted] trade name of this sunscreen product was cancelled by the Patent and Trademark Office on [redacted] and that the product is no longer available in the United States. [redacted] could not find any additional information regarding the [redacted] sunscreen product in the current literature.

[redacted] has determined that FOLEX is the trade name of an injectable methotrexate product. FOLEX is a registered trademark of the Pharmacia & Upjohn Company. Although the product is still included in the "Orange Book", the FOLEX brand is no longer included in the Physicians Desk Reference or in Facts and Comparisons. As a result of conversations held with representatives of Pharmacy & Upjohn and Abbott's Hospital Products Division, a one-time co-marketer of FOLEX, [redacted] has determined that Pharmacia & Upjohn no longer "markets" FOLEX Injectable.

Upon approval, the Dermik product for which the [redacted] mark is requested will be available as a topical fluorouracil cream. It will be administered once a day for the treatment of actinic keratoses of the face and scalp. This product will be prescribed primarily by dermatologists and distributed by retail pharmacies. The product profile of fluorouracil cream differs significantly from that of the FOLEX product. While methotrexate may be prescribed topically for the treatment of psoriasis and rheumatoid arthritis, it is no longer available as the FOLEX brand and would not be generally

available through retail channels. There is no potential for confusion of FOLEX with Dermik's proposed trade name for their fluorouracil cream product.

The results of [redacted] investigation of the trade names [redacted] and FOLEX has led them to conclude that [redacted] and FOLEX Injectable are "no longer available in the market, which would eliminate the possibility of prescribing and dispensing errors".

Thank you for your reconsideration of [redacted] as the brand name for fluorouracil cream.

Information contained within this submission is proprietary and confidential. This information should not be disclosed to any third party without the prior written consent of Dermik Laboratories, Inc. In addition, Dermik considers the contents of this file confidential and exempt from disclosure under 21 C.F.R. § 20.61.

We would appreciate an expeditious review of the study report and the updated name status information that we have submitted in support of the [redacted] trade name we have selected for our fluorouracil cream product.

If you have any questions, please contact me at 610 454-3027.

Sincerely,

James P. Thompson

James P. Thompson
Manager
Regulatory Affairs

JFT/arz
Attachments

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

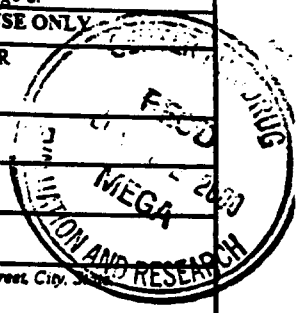
APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

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

Form Approved: OMB No. 0910-0338
*Expiration Date: March 31, 200_*
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
NDA 20-985



APPLICATION INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Dermik Laboratories, Inc.	June 21, 2000
TELEPHONE NO. *(Include Area Code)* (610) 454-3027	FACSIMILE (FAX) Number *(Include Area Code)* (610) 454-5287
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 500 Arcola Road Collegeville, PA 19426	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION synthetic antifungal agent

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* NDA 21-022

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
(fluorouracil cream)	[redacted] Cream 0.5%
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)* 5-fluoro-2,4(1H,3H)-pyrimidinedione	CODE NAME *(If any)* DL-6025

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
	0.5%	topical

(PROPOSED) INDICATION(S) FOR USE: Topical treatment of [redacted]

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
X NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 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)

IF AN ANDA, OR 505(b)(2), 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 ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT X OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: [redacted]

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION Present data and information in support of the [redacted] trade name we have selected for our fluorouracil cream product.

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

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

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
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 Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

See Original Application

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
OPDRA Jerry Phillips

FROM: HFD-540 Vickey Lutwak

	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
26-00		NDA 20-985		

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
——— Cream 0.5%			

NAME OF FIRM:
Dermik Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG EXPERIENCE

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

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Evaluation of tradename: ——— 0.5% and Olux Foam NDA 21-142

NDA 21-142 is a recently approved product, May 30, 2000, in 540. Dr. Jonathan Wilkin would like you to evaluate ——— and Olux for the possibility of name confusion during oral transmission. ——— We will wait for your review before contacting the sponsor about their tradename.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Vickey Lutwak, PM, HFD-540 7-2073	☐ MAIL ☐ HAND
TURE OF RECEIVER	SIGNATURE OF DELIVERER

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

DATE RECEIVED: 7/26/00	DUE DATE: 8/7/00	OPDRA CONSULT #: 00-0202

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

THROUGH:
Vickey Lutwak,
Project Manager
HFD-540

PRODUCT NAME:	**MANUFACTURER:** Dermik Laboratories, Inc.
(fluorouracil cream) 0.5% **NDA #: 20-985**	

SAFETY EVALUATOR: Peter Tam, RPh.

OPDRA RECOMMENDATION:
OPDRA does not recommend the use of the proprietary name, [redacted]

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

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

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

/S/

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

/S/ 8/4/2000

Peter Honig, M.D.
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: 8/4/00

NDA#: 20-985

NAME OF DRUG: ———Cream
(fluorouracil) 0.5%

NDA HOLDER: Dermik Laboratories, Inc.

I. INTRODUCTION:

This consult is in response to a request from the Division of Dermatologic and Dental Drug Products, (HFD-540) to re-review the proposed proprietary name, ——— in regard to recent approval of Olu[redacted], (approved in May 30, 2000) for potential names conflict.

——— was reviewed on 4/3/00 and found unacceptable since an identical product name, ——— suncreen — lotion, is listed in American Drug Index (1999 edition) as well as in USP Drug Information (1999 edition). OPDRA rejected the proposed name since the potential risk is high for an error to occur when there is an identical name for two different products. The firm has since asked OPDRA to re-review the proposed name since ——— is no longer marketed in U.S.

PRODUCT INFORMATION

———cream 0.5% contains 5-fluorouracil, an antineoplastic, antimetabolite product for dermatologic use. It is indicated for the topical treatment of multiple actinic or solar keratoses of the face and scalp.

There is evidence that the metabolism of fluorouracil in anabolic pathway blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this manner, fluorouracil interferes with the synthesis of deoxyribonucleic acid (DNA) and to lesser extent inhibits the formation of ribonucleic acid (RNA). Since DNA and RNA are essential for cell division and growth, the effect of fluorouracil may be to create a thymine deficiency that provokes unbalanced growth and death of the cell. The effects of DNA and RNA deprivation are most marked on those cells which grow more rapidly and take up fluorouracil at a more rapid rate.

Overall, once daily ——— is indictated for the treatment of actinic keratoses or solar keratoses of the face and scalp with at least one week of treatment. Continued treatment for 2 to 4 weeks resulted in further lesion reduction and clearing.

———cream will be supplied in——— 30 gm tubes.

II. RISK ASSESSMENT:

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts[1,2,3] as well as several FDA databases[4] for existing drug names which sound alike or look alike to [redacted] 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]. In addition, OPDRA conducted three aided verbal prescription analysis studies (outpatient), involving health care practitioners within FDA.

[redacted]

[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.

A. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Studies were conducted by OPDRA and involved 88 health professionals comprised of pharmacists, physicians, and nurses within FDA to determine the degree of confusion of [redacted] with Olux due to the similarity in verbal pronunciation of the name. This is designed as an aided study since few would know anything about Olux foam that was approved in May 30,2000. In addition to [redacted] three other similar pronounced drug names are chosen. They are 1) Mycelex, 2) Fluoroplex and 3) Olux. E-mails were sent to all participants with these four drug names. Participants were asked to interpret the verbal prescription order they received against these four choices. A verbal prescription for [redacted] was recorded on voice mail by three different OPDRA's staff. Two spoke with a foreign accent. The voice mail messages were then sent to three different groups of participant health professionals for their interpretation against the four drugs as listed below. Then the participants sent their interpretations of the order via e-mail to the medication error staff.

Product Name	Dosage form(s), Generic name	Usual Dose	Observation
[redacted]	Cream, fluorouracil	Apply to face and neck bid for 2-4 weeks	
Mycelex	Cream, clotrimazole	Apply to affected area bid	*SA
Fluoroplex	Cream, fluorouracil	Apply to face and neck bid for 2-4 weeks	*SA
Olux	Foam, clobetasol	Apply bid	*SA

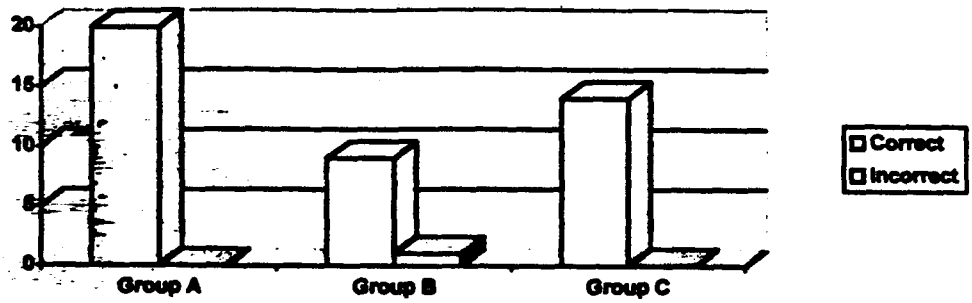
*SA = Sound-alike

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Group A Verbal	30	20(67%)	20	0
Group B Verbal	30	10(33%)	9	1
Group C Verbal	28	14(50%)	14	0
Total	88	44(50%)	43(98%)	1(2%)



Two percent of the participants responded with an incorrect name. The incorrect verbal responses are summarized in Table II

Table II

Group B Verbal	Incorrectly Interpreted
	Olux*

* Existing Product

A. SAFETY EVALUATOR RISK ASSESSMENT

Olux, a recently approved drug, was identified that was thought to have potential for confusion with the proposed name, ——. They sound alike and have similar —— —— and Olux has 4. Both share —— in their name. In addition, they are both used for topical application with overlapping administration intervals at bid.

The results of the verbal prescription studies demonstrated that one (out of forty-three) respondent interpreted —— incorrectly. The incorrect verbal interpretation of the proposed name did overlap with one existing approved product, Olux. This is a significant finding in a study with a small sample size. Based upon this finding within a small study, we object to the use of the proposed name, ——

III. RECOMMENDATIONS:

OPDRA does not recommend the use of the proprietary name, ——.

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.

APPEARS THIS WAY
ON ORIGINAL

/S/ 8/11/00

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

Concur:

/S/ 8/11/00

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

APPEARS THIS WAY
ON ORIGINAL

CC:

NDA – 20-985
Office Files
HFD-540; DivFiles; Victoria Lutwak, Project Manager, DDDDP
HFD-540; Jonathan Wilkin, M.D., Division Director, DDDDP
HFD-042; Patricia Staub, Regulatory Review Officer, DDMAC (Electronic Only)
HFD-430; Patrick Guinn, Project Manager, DDREI, OPDRA (Electronic Only)
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Sammie Beam, Project Manager, OPDRA
HFD-400; Peter Honig, Director, OPDRA (Electronic Only)
HFD-002; Murray Lumpkin, Deputy Center Director for Review Management (Electronic Only)

APPEARS THIS WAY
ON ORIGINAL

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
OPDRA-Request /Tradename 3 rd request	HFD-540 Vickey Lutwak

E	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
15/2000		20-895		

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Formerly [redacted]	PDUFA due date 10/28/00		

NAME OF FIRM: Dermik Laboratories

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG EXPERIENCE

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

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

The sponsor has submitted two tradenames for consideration/evaluation.

1. [redacted]
2. [redacted]

Please not the previous consults for a tradename.

Since the due date is 10-28-00, will need another consult (if these names are good) before the October 28, 2000, due date?

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Lutwak, PM, HFD 540 7-2073 E-MAIL 8/15/00	☒ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

DATE RECEIVED: 8/15/2000	DUE DATE: 10/9/2000	OPDRA CONSULT #: 00-0226

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

THROUGH:
Vicky Lutwak
Project Manager
HFD-540

PRODUCT NAME:	MANUFACTURER: Dermik Laboratories
(fluorouracil cream) 0.5% NDA #: 20-895	

SAFETY EVALUATOR: Peter Tam, RPh.

OPDRA RECOMMENDATION:

OPDRA does not recommend the use of either of the proprietary names, [redacted].

APPEARS THIS WAY
ON ORIGINAL

[/S/] 10/4/2000
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/] 10/5/00
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: 9/25/2000

NDA#: 20-895

NAME OF DRUG: ———
(fluorouracil cream) 5%

NDA HOLDER: Dermik Laboratories

I. INTRODUCTION:

This consult is written in response to a request from the Division of Dermatologic and Dental Drug Products, (HFD-540) received on 8/15/2000 to review the proposed proprietary names, ——— and ———.

The sponsor previously proposed the name ——— for this product. ——— was reviewed on 4/3/00 and found unacceptable since an identical product name, ——— Sunscreen — Lotion, is listed in American Drug Index (1999 edition) as well as in USP Drug Information (1999 edition). OPDRA rejected the proposed name since the potential risk is high for an error to occur when there is an identical name for two different products. The firm later asked OPDRA to re-review the proposed name since ——— is no longer marketed in U.S. However, a recent approved drug, Olux, was identified in a subsequent OPDRA verbal prescription study as a name that could be confused with ——— On these grounds, OPDRA again rejected the name, ———

Therefore, on August 15, 2000, the firm submitted two more names for consideration, ——— and ———.

PRODUCT INFORMATION

——— cream contains 0.5% 5-fluorouracil, an antineoplastic, antimetabolite product for dermatologic use. It is indicated for the topical treatment of multiple actinic or solar keratoses of the face and scalp and is applied once daily for at least one week of treatment. In clinical trials, continued treatment for 2 to 4 weeks resulted in further lesion reduction and clearing. ——— cream will be supplied in ——— 30 gm tubes.

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 ——— 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 for each name (total of 6) 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 names, ——— and ———. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of OPDRA 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. ———

Several product names were identified in the Expert Panel Discussion that were thought to have potential for confusion with ——— The products are listed in the following table.

Product Name	Dosage form(s), Generic name	Usual Dose	Observation
———	Cream, 0.5%, fluorouracil	Apply to face and scalp daily at least for 1 week treatment	
Penlac	Nail lacquer soln, 8%, ciclopirox	Applied to affected nail(s) once daily	*SA/LA
Sulindac	Tablets, 150, 200 mg,	200 mg bid	*SA/LA
Surfak	Capsules, 50, 240 mg, docusate calcium	One capsule as directed	*SA/LA
Similac	Specialized infant food	As directed	*SA/LA

*SA = Sound-alike
*LA = Look-alike

[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.

Penlac, Sulindac, Surfak and Similac were the product names that were identified to have the most potential confusion with ———. These products all look-alike and sound-alike relative to ——— The panel concluded that the above listed drugs and ——— were likely to be confused with each other, possibly resulting in medication errors.

2. ———

This second proposed name differs only by the ——————— (in ———. The potential for medication errors due to name confusion among these same products as discussed above with the proposed name, ———, also seems likely.

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 ——— or ——— 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 ——— or ——— 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.

1. ———Rx

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: ——— #1 Sig: Use daily as directed	——— #1 Sig: Use daily as directed
Inpatient RX: ———qd as directed	

2. ——— Rx

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: ———#1 Sig: Use daily as directed	———#1 Sig: Use daily as directed
Inpatient RX: ———qd as directed	

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Outpatient	29	20(69%)	11	9
Verbal	30	19(63%)	1	18
Written Inpatient	31	15(48%)	10	5
Total	90	54(60%)	22(41%)	32(59%)
Written Outpatient	29	20(69%)	18	2
Verbal	30	17(57%)	12	5
Written Inpatient	31	15(48%)	13	2
Total	90	52(58%)	43(83%)	9(17%)

a. ———

59 percent of the participants responded with an incorrect name. The incorrect written and verbal responses are summarized in Table II.

b. ———

17 percent of the participants responded with an incorrect name. The incorrect written and verbal responses are summarized in Table II.

Table II

	Incorrectly Interpreted
Written Outpatient	
Verbal	
	*Sulindac (2)
Written Inpatient	*Sintab
	*Surfak (3)
Written Outpatient	*Similac
	*Simlac

Verbal		*Sulindac
Written Inpatient		*Surfak
	*Simlac	

* Existing Marketed Product – Sulindac, Sinutab (spelled as Sintab), Surfak, Similac (spelled as Simlac)

C. SAFETY EVALUATOR RISK ASSESSMENT

Since ——— and ——— are so similar in spelling and pronunciation, they could be considered as one proposed proprietary name. In fact, many respondents in both studies interpreted ——— as ——— or vice versa.

Several proprietary product names were identified in the Expert Panel that were thought to have potential for confusion with the proposed name, ——— and ——— They are Sulindac, Surfak, Penlac and Similac. Of the four, Similac poses less potential for confusion since it is not a prescription drug but an infant food. The other three products, Penlac, Sulindac, and Surfak have sound-alike and look-alike properties when compared to ——— or ——— In addition, Penlac and ——— or ——— have overlapping dosage forms and dosing frequency (once daily). Penlac is available as topical solution and ——— or ——— is supplied as topical cream. Hence, the potential risk for medication errors due to name confusion among these products seems likely.

Results of the first study (———) indicate that thirty-two respondents interpreted ——— incorrectly. Several of these inaccurate interpretations of the proposed name, ———, overlapped with 3 existing drug products: Sulindac (n =2), Surfak (n = 3) and "Sintab" (n =1, presumably "Sinutab").

Results of the second study (———) indicate that nine respondents interpreted ———incorrectly. Several of these inaccurate interpretations of the proposed name,———, overlapped also with 3 existing products: Similac (n =3, one as "Simlac" presumably for Similac), Sulindac (n =1), and Surfak (n =1).

In summary, although none of the overlapping existing drug products (Sulindac, Surfak, Sinutab) that we found in our prescription studies share any common indications, dosage forms (cream vs tablets and capsules) or administration schedule with——— or——— we consider this a significant finding. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population. Also, the Expert Panel believed the newly approved "Penlac" poses a potential risk for medication errors. In addition to their sound-alike and look-alike qualities, Penlac and ——— are available as topical preparations and applied once daily. Past post-marketing experience has demonstrated that products that have overlapping properties such as similar dosage forms and dosing intervals increase the potential risk for medication errors.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

Please see Consult # 00-00016.

IV. RECOMMENDATIONS:

OPDRA does not recommend the use either of the proprietary names, [redacted]

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/ 9/29/00

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

Concur:

/S/ 10/4/2000

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

APPEARS THIS WAY
ON ORIGINAL

CC:

NDA – 20-895
HFD-540; DivFiles; Vicky Lutwak, Project Manager
HFD-540; Jonathan Wilkin, M.D. Division Director
HFD-400; Jerry Phillips, Associate Director, OPDRA
HFD-400; Peter Tam, Safety Evaluator, OPDRA

Electronic only cc:

HFD-400; Sammie Beam, Project Manager, OPDRA
HFD-042; Patricia Staub, Regulatory Review Officer, DDMAC
HFD-430; Patrick Guinn, DDREI, OPDRA
HFD-002; Murray Lumpkin, Deputy Center Director for Review Management
HFD-400; Peter Honig, Director, OPDRA

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APPEARS THIS WAY
ON ORIGINAL

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:		FROM:	
OPDRA Jerry Phillips		HFD-540 Vickey Lutwak	
DATE 10-17-00	IND NO.	NDA NO. NDA 20-985	TYPE OF DOCUMENT	DATE OF DOCUMENT
NAME OF DRUG Fluorouracil 0.5%, Cream	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE Priority

NAME OF FIRM:
Dermik Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

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

II. BIOMETRICS

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

III. BIOPHARMACEUTICS

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

IV. DRUG EXPERIENCE

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

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Evaluation of tradenames:
1. CARAC
2. _____

~~Will be sent by mail~~

E-mailed
10/17-00

SIGNATURE OF REQUESTER Lutwak, PM, HFD-540 7-2073	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-985

DEC 2 1999

Dermik Laboratories, Inc
Attention: Ronald F. Panner
Senior Director, Worldwide Regulatory Affairs
500 Arcola Road
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] (fluorouracil) Cream, 0.5%

Therapeutic Classification: Standard (S)

Date of Application: October 28, 1999

Date of Receipt: October 28, 1999

Our Reference Number: NDA 20-985

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 December 27, 1999 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be August 28, 2000 and the secondary user fee goal date will be October 28, 2000.

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 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

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 notify you within 120 days of receipt of your response whether a waiver is granted. 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 proceed with the pediatric drug development plan that you submit and notify you of the pediatric studies that are required under section 21 CFR 314.55. 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

If you have any questions, contact Victoria Lutwak, Project Manager, at 301-827-2020.

Sincerely,

[/S/]

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 20-985
HFD-540/Div. Files
HFD-540/V.Lutwak
HFD-540/S.Walker
HFD-540/A.Jacobs
HFD-540/DeCamp

DISTRICT OFFICE

APPEARS THIS WAY
ON ORIGINAL

Drafted by: smc/November 2, 1999
filename: N20985.ACK

ACKNOWLEDGEMENT (AC)

Item 19A: Pediatric Use Waiver

In accordance with 21 CFR§314.55(c), Dermik Laboratories, Inc. hereby requests a full waiver of the requirements of 314.55 paragraph (a) because [redacted] Cream 0.5% (fluorouracil cream) is not likely to be used in a substantial number of pediatric patients for the topical treatment of multiple actinic or solar keratosis of the face and scalp.

APPEARS THIS WAY
ON ORIGINAL