CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-985

CORRESPONDENCE

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

APPLICATION INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Dermik Laboratories, Inc.	October 28, 1999
TELEPHONE NO. (Include Area Code)	FACSIMILE (FAX) Number (Include Area Code)
(610) 454-3026	(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 (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE
500 Arcola Road 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
(fluorouracil cream)	Cream 0.5%
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any)	CODE NAME (if any)
5-fluoro-2,4(1H,3H)-pyrimidinedione	DL 6025

DOSAGE FORM:	STRENGTH:	ROUTE OF ADMINISTRATION:
topical cream	0.5%	topical

(PROPOSED) INDICATION(S) FOR USE: Topical treatment of multiple actinic or solar keratosis of the face and scalp

APPLICATION INFORMATION

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

REASON FOR SUBMISSION Original New Drug Application

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

NUMBER OF VOLUMES SUBMITTED 33 THIS APPLICATION IS PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

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

See Attached

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

See Attached

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

CERTIFICATION

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

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

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Ronald F. Panner	Ronald F. Panner, Senior Director Worldwide Regulatory Affairs	10/28/99

ADDRESS (Street, City, State, and ZIP Code)	Telephone Number
500 Arcola Road Collegeville, PA 19426	(610) 454-3026

NDA 20-985
17-Oct-2000

Questions Regarding Phase IV commitment for Dermik's fluorouracil cream, 0.5%

The following questions are to clarify the Phase IV commitments requested by DDDDP in a letter that was faxed to Dermik on October 13, 2000.

1. Please provide clarification explaining specifically how the number of subjects studied does not reach the numbers recommended in the ICH EIA guidance and advice Dermik as to what the FDA would like Dermik to do in order to fulfill this request.

2. Are all of the Phase IV requests required to be collected in one study? Is there a priority or sequence in which the FDA would like Dermik to fulfill the commitment?

3. Dermik would like to discuss potential study designs with respect to:

- The number of patients that might fulfill the additional safety data and informational needs request for treatment of common skin surface areas

- How best to examine the specific questions of clinical interest (different areas of skin, recurrence, re-treatment, minimizing eye-irritation)

Dermik would like to have a clinical dialog with the FDA regarding the above mentioned points and thanks the FDA in advance for taking the time to discuss these questions.

APPEARS THIS WAY
ON ORIGINAL

Sponsor's Proposed
PPI

APPEARS THIS WAY
ON ORIGINAL

WITHHOLD 1 PAGE (S)

Draft

Labeling

PLEASE NOTE:

Since the sponsor has no tradename at the time of action, I have chosen to leave the tube and carton labels that were in the original NDA in the action package. See section under TRADENAME.

When they do have a tradename, the sponsor will submit a SLR to the NDA with new art work/logo/etc..
VL

WITHHOLD 57 PAGE (S)

Draft

Labeling

ORIGINAL

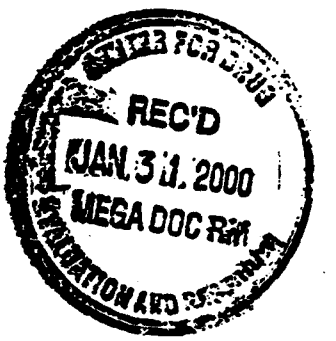
DERMIK LABORATORIES, INC.
A RHONE-POULENC RORER COMPANY
Dedicated to Dermatology

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

NEW CORRESP
NC

January 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



NDA 20-985
[redacted] Cream 0.5%
(fluorouracil cream)

Amendment to a Pending Application

Dear Dr. Wilkin:

Reference is made to your December 2, 1999 letter acknowledging receipt of our New Drug Application for [redacted] Cream.

In the letter, you provided us with the pediatric study requirements and informed us that our waiver request with supporting information and documentation should be submitted within 60 days of receipt of your December 2, 1999 letter.

This submission addresses our request for a waiver of the pediatric study requirement which was included in our original October 28, 1999 NDA submission.

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

Sincerely yours,

Ronald F. Panner

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/jpt/maf
Enclosures

BEST POSSIBLE COPY

Desk Copy: Ms. Vickey Lutwak, Project Manager

NOTE: 2nd copy of letter for VL as a desk copy.

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

REQUEST FOR CONSULTATION

(Division/Office):			FROM:	
OPDRA Jerry Phillips			HFD-540 Vickey Lutwak	
DATE	**IND NO.**	**NDA NO.**	**TYPE OF DOCUMENT**	**DATE OF DOCUMENT**
1-7-00		NDA 20-985		
NAME OF DRUG	**PRIORITY CONSIDERATION**		**CLASSIFICATION OF DRUG**	**DESIRED COMPLETION DATE**
——— Cream 0.5%				

NAME OF FIRM:
Dermik Laboratories, Inc.

Please e-mail that this arrived - Thanks - /s/

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

'LETTER

IDENCE

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL AF
☐ 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 tradename: ——— 0.5%
Draft Tube and Carton labels included——— 30 gram size

Will be sent by mail

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

The following names were used during development for the 0.5% fluorouracil topical cream, which is the subject of this original NDA. The technical reports and documents in this NDA contain several different names for the 0.5% fluorouracil topical cream. These are listed below.

0.5% FU Cream
5-FU 0.5% cream
5-Fluorouracil cream
5-Fluorouracil 0.5% Topical Cream
5-fluorouracil cream 0.5%
5-Fluorouracil Cream 0.5%
0.5% 5-FU cream with Microsponge®
— FU
— 5-FU
— 5-FU (0.5%) Topical Cream
— 5-Fluorouracil (5-FU) 0.5% Cream
Dermik 5-FU
Dermik 5-FU 0.5% cream
Dermik's 5-FU 0.5% cream
DL6025
Experimental 0.5% 5-FU Formulation
fluorouracil 0.5% cream

The tradename for this product is ———— This name only appears in the proposed package insert and product labeling in this original NDA.

APPEARS THIS WAY
ON ORIGINAL

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

REQUEST FOR CONSULTATION

Division/Office): Peter Cooney			FROM: Vickey Lutwak HDF540 7-2073	
DATE Dec 8, 1999	IND NO.	NDA NO. 20-985	TYPE OF DOCUMENT NDA	DATE OF DOCUMENT Oct 28, 1999
NAME OF DRUG 5 Fluorouracil	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE

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
- ☐ 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

Consult for review

SIGNATURE OF REQUESTER Victoria Lutwak	METHOD OF DELIVERY (Check one) ☐ 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

October 28, 1999

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. 20-985
——— Cream 0.5%
(fluorouracil cream)

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 ——— Cream 0.5% (fluorouracil cream) which demonstrates the efficacy and safety of the product in the topical treatment of patients with multiple actinic or solar keratosis of the face and scalp.

This application contains the following sections: 1) Index, 2) Draft Labeling, 3) Application Summary, 4) Chemistry, Manufacturing and Controls (Including Sample Information and 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) Patient Certification, 16) Debarment Certification, 17) Field Copy Certification, 18) User Fee Cover Sheet, and 19A) Pediatric Use Waiver, and 19B) Financial Disclosure Information.

Information is also included in electronic format consisting of SAS datasets for the pivotal clinical trials, and electronic copies of final study reports for the phase III trials and the integrated summaries. This information is contained on diskettes attached in the first volume of this NDA submission (Item 3, Volume 1, Page 168). No computer viruses were detected when these disks were scanned using ——— Software, LTD Version —

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

October 28, 1999

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

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 [redacted] Cream 0.5% (fluorouracil cream) which demonstrates the efficacy and safety of the product in the topical treatment of patients with multiple actinic or solar keratosis of the face and scalp.

This application contains the following sections: 1) Index, 2) Draft Labeling, 3) Application Summary, 4) Chemistry, Manufacturing and Controls (Including Sample Information and 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) Patient Certification, 16) Debarment Certification, 17) Field Copy Certification, 18) User Fee Cover Sheet, and 19A) Pediatric Use Waiver, and 19B) Financial Disclosure Information.

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In accordance with the Prescription Drug Use Fee Act of 1992, a check No. ——, in the amount of $272,282.00 was sent to the Food and Drug Administration, Pittsburgh, Pennsylvania on October 12, 1999. This application was assigned User Fee Identification Number 3825.

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 306(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,

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/JPT/maf
Enclosures

APPEARS THIS WAY
ON ORIGINAL

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

NEW CORRESP

NC

December 7, 1999

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

Response to FDA Request for Information

Dear Dr. Wilkin,

Reference is made to several telephone conversations with Ms. Vickey Lutwak on December 1, 1999 about our recently submitted NDA for——— (fluorouracil cream) ———Cream 0.5%. Ms. Lutwak requested additional information as itemized on the attached list.

This amendment responds to three of Ms. Lutwak's requests. Our response to the request for references for the annotated labeling will be submitted shortly.

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

Sincerely,

James P. Thompson

James P. Thompson
Manager
Worldwide Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Response to FDA/DDDDP
Request for Information

1. DDDDP Request: Please provide us with additional desk copies of Volumes 1.30, 1.31, 1.32 and 1.33 from the ——— Cream NDA.

Dermik Response: Included in this submission are copies of the requested four volumes. There are two sets of the four volumes. One set is for the Clinical Reviewer. The other set is for the Statistical Reviewer.

2. DDDDP Request: Please provide us with a desk copy of Volume 1.5 of the ——— Cream NDA.

Dermik Response: Included in this submission is a desk copy of Volume 1.5 (Methods Validation) of the application.

3. DDDDP Request:

- Please provide the full references referred to in the annotated label.
- Annotate and provide the full references used for the description of the teratogenicity associated with 5-fluorouracil;
- Annotate and provide the full references used for the information provided in the carcinogenesis, mutagenesis and impairment of fertility section of the label;
- Provide the estimate of maximum daily human topical dose in mg/kg and mg/m^2 that was used for calculating fold exposure levels in the label.

Dermik Response: A response will be provided shortly.

4. DDDDP Request: Please provide electronic copies of the SAS data sets for the Reviewing Statistician.

Dermik Response: Included in this submission are 2 electronic copies (disks) of the SAS Data Sets you requested. One disk is for the Archival Copy of the NDA. It should be placed in the plastic disk holder located at the end of Volume 1. The other disk belongs in the Review Copy of the NDA. This copy of the SAS Data Sets should be given to the Statistical Reviewer.

/7/99

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APPEARS THIS WAY
ON 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

December 10, 1999

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 20-985
_____ Cream 0.5%
(fluorouracil cream)

Amendment to a Pending Application

Dear Dr. Wilkin,

Reference is made to our original New Drug Application for _____ (fluorouracil) Cream 0.5% that was submitted by Dermik and received at the Divison of Dermatologic and Dental Drug Products on October 28, 1999.

A typographical error has been detected in four tables containing the same information. In these tables, information pertaining to study DL6025-9715 was inadvertently provided for study DL6025-9815. The tables have been corrected and clarification of the Age, Sex and Race column are also provided. Enclosed please find replacement pages which contain the wording "Revised 12/2/99" under the NDA page number for insertion into the appropriate volumes. One table is found in Item 3, the Overall NDA Summary, and three of the tables are in Item 8, the clinical data section of NDA #20-985 and are located on the following NDA pages:

NDA Volume Number	Item - Volume - Page Number (NDA Item No. - Item Volume No. - Volume Page No.)
1.1	3-1-85
1.17	8-1-4
1.17	8-1-8
1.17	8-1-32

ORIGINAL

Three sets of corrected pages, one for the Archival Copy and one set each for the Clinical and Statistical Review Copy of the NDA, are enclosed. Also enclosed are 15 desk copies of the replacement table for Volume 1.1. We apologize for any inconvenience this may cause.

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

Sincerely yours,

James F. Thompson /for

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/jpt/maf
Enclosures

APPEARS THIS WAY
ON 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

December 10, 1999

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

Amendment to a Pending Application

Dear Dr. Wilkin,

Reference is made to our original New Drug Application for ———— (fluorouracil) Cream 0.5% that was submitted by Dermik and received at the Divison of Dermatologic and Dental Drug Products on October 28, 1999.

A typographical error has been detected in four tables containing the same information. In these tables, information pertaining to study DL6025-9715 was inadvertently provided for study DL6025-9815. The tables have been corrected and clarification of the Age, Sex and Race column are also provided. Enclosed please find replacement pages which contain the wording "Revised 12/2/99" under the NDA page number for insertion into the appropriate volumes. One table is found in Item 3, the Overall NDA Summary, and three of the tables are in Item 8, the clinical data section of NDA #20-985 and are located on the following NDA pages:

NDA Volume Number	Item - Volume - Page Number (NDA Item No. - Item Volume No. - Volume Page No.)
1.1	3-1-85
1.17	8-1-4
1.17	8-1-8
1.17	8-1-32

Three sets of corrected pages, one for the Archival Copy and one set each for the Clinical and Statistical Review Copy of the NDA, are enclosed. Also enclosed are 15 desk copies of the replacement table for Volume 1.1. We apologize for any inconvenience this may cause.

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

Sincerely yours,

James F. Thompson /for

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/jpt/maf
Enclosures

Desk Copy: Ms. Vickey Lutwak, Project Manager

APPEARS THIS WAY
ON 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

BC

January 18, 2000

JAN 20 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

———— Cream, 0.5%
(fluorouracil cream)

NDA #20,985

INFORMATION AMENDMENT:
Chemistry, Manufacturing and Controls

Dear Dr. Wilkin,

Reference is made to our October 18, 1999 New Drug Application containing, in part, CMC information for ———— Cream, 0.5% (fluorouracil cream).

Included in this submission is the 12-Month Interim Stability Report for 5-Fluorouracil Cream, 0.5%. Packaged in ———— 30 Gram HDPE Tubes. All stability data is within the proposed product specifications. Please note the corrections in the stability data tables for transcription errors in some of the 9 month methylparaben and propylparaben data previously filed in the October 18, 1999 original NDA. The corrected values have been bolded in tables 3 - 5 and 9 - 11 for your convenience.

If you have any questions or comments regarding this submission, please contact me at (610) 454-3034 or James Thompson at (610) 454-3027.

ORIGINAL

Sincerely,

Jo Anne Calleri
Manager, CMC Liaison
Worldwide Regulatory Affairs

Enclosures

cc: 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

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

January 18, 2000

BL

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

Amendment to a Pending Application

Dear Dr. Wilkin:

Reference is made to a December 1, 1999 facsimile transmission from Project Manager Ms. Vickey Lutwak commenting on our pending New Drug Application for [redacted] Cream.

This submission responds to Ms. Lutwak's comments.

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

Sincerely yours,

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/jpt/maf
Enclosures

Desk Copy: Ms. Vickey Lutwak, Project Manager

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

APPLICATION INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Dermik Laboratories, Inc.	January 18, 2000
TELEPHONE NO. (*Include Area Code*)	**FACSIMILE (FAX) Number (*Include Area Code*)**
(610) 454-3026	(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 (*Number, Street, City, State, 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 20-468

ESTABLISHED NAME (*e.g., Proper name, USP, USAN name*)	PROPRIETARY NAME (*trade name*) IF ANY
(fluorouracil cream)	Cream 0.5%
CHEMICAL, BIOCHEMICAL, BLOOD PRODUCT NAME (*If any*)	**CODE NAME (*If any*)**
5-fluoro-2,4(1H,3H)-pyrmidinedione	DL-6025
DOSAGE FORM: Intranasal Spray cream	**STRENGTHS** 0.5%	**ROUTE OF ADMINISTRATION:** topical

(PROPOSED) INDICATION(S) FOR USE: Topical treatment of multiple actinic or solar keratosis of the face and scalp

APPLICATION INFORMATION

APPLICATION TYPE (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) ☐ 50

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 OTHER

REASON FOR SUBMISSION: Amendment to a Pending Application

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

NUMBER OF VOLUMES SUBMITTED: —

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 NDA

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

See Original NDA

Response to FDA/DDDDP
Request for Information

FDA Comment:

It is requested that the sponsor provide the full references referred to in the annotated label. Reference numbers are listed in the annotated label, but there is no reference list provided to match the numbers. In addition, it is requested that the sponsor annotate and provide the full references used for the description of the teratogenicity associated with 5-fluorouracil provided in the label. Also, it is requested that the sponsor annotate and provide the full references used for the information provided in the carcinogenesis, mutagenesis and impairment of fertility section of the label.

Dermik Response:

Attached is a copy of the full prescribing information for ———— Cream that has been revised as requested by Ms. Lutwak.

FDA Comment:

It is requested that the sponsor provide the estimate of maximum daily human topical dose in mg/kg and mg/m^2 that was used for calculating fold exposure levels in the label.

Dermik Response:

Anticipated maximum clinical dose =
2.0 g cream per 50 kg person per day =
40 mg/kg of 0.5% cream = **0.2 mg/kg/day 5-FU.**

km (surface area conversion factor) for humans = 37[1]

mg/m^2 = 0.2 mg/kg x 37 = 7.4 mg/m^2/day.

[1]Freireich, E.J., et al., 1966. Quantitative comparison of toxicity of anticancer agents in mouse, rat, hamster, dog, monkey and man. *Cancer Chemotherapy Reports.* 50:219-244.

ORIGINAL NEW CORRESP

NC

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 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

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

Amendment to a Pending Application

Dear Dr. Wilkin:

Reference is made to your December 2, 1999 letter acknowledging receipt of our New Drug Application for ———— Cream.

In the letter, you provided us with the pediatric study requirements and informed us that our waiver request with supporting information and documentation should be submitted within 60 days of receipt of your December 2, 1999 letter.

This submission addresses our request for a waiver of the pediatric study requirement which was included in our original October 28, 1999 NDA submission.

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

Sincerely yours,

Ronald F. Panner

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

RFP/jpt/maf
Enclosures

Desk Copy: Ms. Vickey Lutwak, Project Manager

WK- original copy
next letter desk copy - bg-ic

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

Pediatric Use Waiver

Please refer to Dermik's October 28, 1999 original NDA filing for ———— (fluorouracil cream) Cream 0.5% which contains Dermik's request for a full waiver of the pediatric study requirement. The waiver request is located on page 1-1-10 of Volume 1. A duplicate copy of our waiver request from the original NDA submission is included in this submission as an attachment.

Also included in this submission is a printout of data from the ———— for actinic keratosis treatment by modality (termed "uses") and patient age, for a one-year period ending November 1999. This printout was not included in the original NDA filing. The data reflect 1,838,000 modality uses to treat actinic keratosis in this period. The lowest demographic catagory of patients with any modality use reported is age 11 to 20 years. The —— reported the following uses by modality for this demographic category:

	MAT/NO/99 Uses (000)
Liquid Nitrogen	3
Retin-A	3
Erythromycin Base	3
Cleocin-T	3

Overall, patients in this lowest demographic category accounted for a small percentage of modality uses to treat actinic keratosis. It is concluded that ———— Cream 0.5% is not likely to be used in a substantial number of pediatric patients for the treatment of multiple actinic or solar keratosis of the face and scalp.

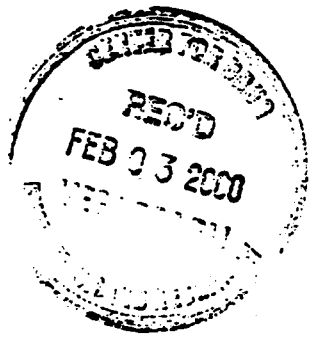
DERMIK LABORATORIES, INC.
Dedicated to Dermatology
A RHÔNE-POULENC RORER COMPANY

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

Febuary 1, 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 20-985
[redacted] Cream 0.5%
(fluorouracil cream)

Response to FDA Request for Information

Dear Dr. Wilkin,

Reference is made to a January 18, 2000 telephone call from DDDDP Project Manager Ms. Victoria Lutwak requesting additional copies of Volumes 1.4 and 1.5 of the original NDA for [redacted] (fluorouracil cream) [redacted] Cream 0.5%. Ms. Lutwak asked that these volumes be sent directly to the Microbiologist Reviewer, Bryan Riley, at the Parklawn Building.

As requested by Ms. Lutwak, the requested volumes were sent to Mr. Riley via overnight mail as of the date of this letter.

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

Sincerely,

Ronald F. Panner
Senior Director
Worldwide Regulatory Affairs

2 Desk Copies: Mr. Bryan Riley, Microbiologist, Office of New Drug Chemistry

ORIGINAL
NDA ORIG AMENDMENT
BM

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

ARCOLA ROAD
O. BOX 1200
OLLEGEVILLE, PA 19426-0107
EL. 610-454-8000

March 3, 2000

onathan K. Wilkin, M.D.
irector
ivision of Dematologic and Dental Drug Products,
FD-540
enter for Drug Evaluation and Research
ood and Drug Administration
201 Corporate Blvd.
ockville, MD 20850-3202

CENTER FOR DRUG EVALUATION AND RESEARCH
MAR. VL.
REC'D
~~FEB~~ 17 2000
MEGA DOC RM

This date is corrected on the archival copy.
VL

NDA 20-985
_____ Cream
(fluorouracil cream) 0.5%

Amendment to a Pending Applica
FDA Request for Information

Dear Dr. Wilkin,

Reference is made to a February 23, 2000 telephone call from Project Manager Ms. Vickey Lutwak concerning Dermik's NDA for _____ Cream (fluorouracil cream) 0.5%. During our conversation Ms. Lutwak requested the submission of specified clinical data already included in our application on a CD Rom. This request was made for the Medical Reviewer.

Included in this submission is a CD Rom containing the requested information.

Please note that the SAS data sets are not being submitted on a CD Rom at this time. Dermik will submit the SAS data sets on a CD Rom when the reviewing statistician confirms that the computer disc originally submitted is properly formatted as discussed at the Pre-NDA meeting held July 26, 1999.

If Dermik can provide you with any additional information, please contact me at 610 454-3027.

Sincerely,

James P. Thompson

James P. Thompson
Manager
Worldwide Regulatory Affairs

JPT/arz
Attachments

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

AMENDMENT
BC

June 9, 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 20-985
——— Cream 0.5%
(fluorouracil cream)

INFORMATION AMENDMENT:
Chemistry, Manufacturing and Controls

Dear Dr. Wilkin,

Reference is made to our October 18, 1999 New Drug Application containing, in part, CMC information for ——— Cream, 0.5% (fluorouracil cream). Reference is also made to our January 18, 2000 Information Amendment updating this application with a 12-Month Interim Stability Report for ——— Cream.

Included in this submission is the 18-month Interim Stability Report for ——— Cream, 0.5%, Packaged in ——— 30 Gram HDPE Tubes. All stability data is within the proposed product specifications.

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/maf
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

NDA ORIG AMENDMENT

June 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

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

Response to FDA Request for Information

Dear Dr. Wilkin,

Reference is made to a June 6, 2000 fax we received from DDDDP Project Manager Ms. Victoria Lutwak requesting additional information for the ——— (fluorouracil cream) Cream 0.5% reviewers.

Included in this submission is Dermik Laboratories, Inc.'s response to Ms. Lutwak's request.

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/maf
Enclosures

ORIGINAL

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

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

June 26, 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

AMENDMENT
BC

——— Cream, 0.5%
(fluorouracil cream)

NDA #20,985

INFORMATION AMENDMENT:
Chemistry, Manufacturing and Controls

Dear Dr. Wilkin,

Reference is made to our October 18, 1999 New Drug Application containing, in part, CMC information for ——— Cream, 0.5% (fluorouracil cream).

A Pre-Approval inspection of our contract manufacturer, Pharmaceutical Manufacturing Research Services, Inc., was conducted on June 15, 16, 19, 20, 2000. The FDA Investigator, Ms. Debra J. Bennett of the Montgomeryville, PA field office, requested that Dermik amend the pending NDA to include a proposed master manufacturing and packaging batch record. Included in this submission are the proposed master batch record and a copy of the Dermik letter of commitment, as provided to Investigator Bennett during the inspection.

If you have any questions or comments regarding this submission, please contact me at (610) 454-8094 or James Thompson at (610) 454-3027.

Sincerely,

Edward J. Smith

Edward J. Smith
Manager, CMC
Drug Regulatory Affairs

BEST POSSIBLE COPY

ORIGINAL

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

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

NDA ORIG AMENDMENT

July 7, 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 20-985
——— Cream 0.5%
(fluorouracil cream)

Amendment to a Pending Application
Response to FDA Request for Information

Dear Dr. Wilkin:

Reference is made to a June 26, 2000 telephone call from Consumer Safety Officer Ms. Victoria L. Lutwak requesting Dermik to prepare and submit draft patient instructions for ——— (fluorouracil cream) ——— Cream 0.5%. Ms. Lutwak also requested an electronic copy of the same instructions on a computer disk.

Included in this submission are the draft patient instructions Ms. Lutwak requested. These draft instructions are the same as those that were faxed to Ms. Lutwak on June 30, 2000. Also included is an electronic copy (disk) of the same draft instructions.

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/arz
Enclosures
Desk Copy: Ms. Victoria L. Lutwak, Project Manager

ORIGINAL

Facsimile Cover Page

Date: 21 June 2000

To:	Ms. Victoria Lutwak
Company:	FDA
Department:	DDDDP
Phone #:	301-827-2073
Fax Number:	301-827-2075

From:	Jim Thompson
Department:	Regulatory Affairs
Phone #:	610-454-3027
Fax Number:	610-454-5287
Pages Sent:	15

Subject: NDA 20-985. [redacted] (fluorouracil cream)

Attached is Dermik's response to your June 20, 2000 fax memo commenting on our [redacted] NDA. An official submission containing the same information will be made tomorrow.

APPEARS THIS WAY
ON 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

AMENDMENT

BC

July 14, 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 No. 20-985
[redacted] Cream, 0.5%
(fluorouracil cream)

INFORMATION AMENDMENT:
Chemistry, Manufacturing and Controls

Dear Dr. Wilkin,

Reference is made to our New Drug Application dated October 28, 1999 which contained, in part, CMC information for [redacted] Cream, 0.5% (fluorouracil cream).

[redacted] the supplier of the [redacted] has informed Dermik in a March 31, 2000 letter that their Drug Master File No. [redacted] was amended. We have been told that this DMF amendment provides for a [redacted] The resulting [redacted] product meets all specifications required by USP.

This letter serves as an amendment to the Chemistry, Manufacturing and Controls section of the [redacted] Cream NDA No. 20-985.

If you have any questions or comments regarding this submission, please contact me at (610) 454-3027.

Sincerely,

James P. Thompson

James P. Thompson
Manager
Worldwide Regulatory Affairs

cc: 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

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

NDA ORIG AMENDMENT

August 2, 2000

Jonathan Wilkin, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products (HFD-540)
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

BM

NDA No. 20-985

[redacted] Cream, 0.5%
(fluorouracil cream)

Amendment to a Pending Application
Response to FDA Request for Information

Dear Dr. Wilkin:

Reference is made to the facsimile dated July 31, 2000 we received from DDDDP Project Manager Ms. Victoria Lutwak requesting additional information for the [redacted] (fluorouracil cream) Cream 0.5% medical reviewer.

Included in this submission is Dermik's response to Ms. Lutwak's request.

Thank you for your attention. Please contact me at (610) 454-3027 if you have any questions.

Sincerely,

James P. Thompson

James P. Thompson
Regulatory Manager
Worldwide Regulatory Affairs

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

August 4, 2000

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

NDA 20-985
[redacted] Cream 0.5%
(fluorouracil cream)

CHANGE OF ADDRESS

Dear Dr. Wilkin:

Reference is made to our New Drug Application for [redacted] Cream 0.5% (fluorouracil cream).

Please be advised that, effective August 16, 2000, Dermik Laboratories, Inc., the sponsor of the referenced NDA, will move from their Collegeville, Pennsylvania facility to a new facility in Berwyn, Pennsylvania. Our new address is:

Dermik Laboratories, Inc.
1050 Westlakes Drive
Berwyn, PA 19312

Also, please be aware that during a five-day period beginning Friday, August 11, 2000 and ending Tuesday, August 15, 2000, Dermik's office telephones and fax machine will be out of service. However, Ms. Alina Ziglinski, a Dermik representative, will be available for telephone calls at (610) 454-3033 and fax messages can be sent to (610) 454-5287.

I will continue to be the primary FDA contact person for Dermik. In addition, Alicia Cabrelli is also authorized as a Dermik contact person. Her telephone number is (484) 595-2775. My new telephone number is (484) 595-2795 and our new fax number is (484) 595-2785.

If you have any questions regarding our relocation or the referenced application, please feel free to contact me at the above listed telephone number.

Sincerely,

James P. Thompson

James P. Thompson
Manager, Regulatory Affairs

Dermik Laboratories, Inc.
Facsimile Cover Page

Date: August 14, 2000

To: Ms. Victoria Lutwak
Project Manager
Fax Number: 301 827-2075

From: James P. Thompson
Manager, Regulatory Affairs
Phone #: 610 454-3027
Fax Number: 610 454-5287

Pages Sent: 1

Vicky,

The names that follow are the trade names we are proposing for our fluorouracil product in order of preference

1. [ ]
2. [ ]

Please call me at 610 454-3027 if you have any questions. I can be reached at this number tomorrow also.

James P. Thompson

DERMIK LABORATORIES, INC. — *A RHÔNE-POULENC RORER COMPANY*

Dedicated to Dermatology

1050 Westlakes Drive
Berwyn, PA 19312

Alicia Cabrelli
Regulatory Analyst

TEL. ++ 484-595-2775
FAX: ++ 484-595-2785

cc
Okun
Vaughan
DeCamp
Hathaway

FAX TRANSMISSION

DATE & TIME:	09/29/00 11:17 AM
TO:	Vickey Lutwak, Project Manager
COMPANY:	Food and Drug Administration
FAX:	301-827-2075
RE:	**NDA 20-985** [redacted] **Cream, 0.5%** **(fluorouracil cream)**
PAGES:	5 pgs

NOTE — !! My question was #2 — They added #1 & 3 VL

Confidential: For Your Eyes Only

Dear Vickey-

Per your voice mail message to Jim Thompson on September 29, 2000, attached for the Division's review are the following documents referencing the above referenced NDA.

1. *Package Insert Pg. 1: Change from* [redacted] *to "methyl methacrylate/glycol dimethacrylate crosspolymer".*
2. *Package Insert Pg. 8: Delete "*[redacted]*" Change "Collegeville, PA 19426 USA" to "Berwyn, PA 19312, USA".*
3. *Copy of letter from Cosmetic, Toiletry, and Fragrance Association (CTFA) regarding the change in the International Nomenclature Cosmetic Ingredient (ICNC) name for the microsponge.*

If you have any questions, please feel free to contact me at 484-595-2775.

Kind regards,

Alicia Cabrelli

Alicia Cabrelli

BEST POSSIBLE COPY

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

1050 Westlakes Drive
Berwyn, PA 19312

Alicia Cabrelli
Regulatory Analyst

TEL. ++ 484-595-2775
FAX: ++ 484-595-2785

CC
Okun
Vaughan
Dockemp
Hattaway

FAX TRANSMISSION

DATE & TIME: 09/29/00 11:17 AM
TO: Vickey Lutwak, Project Manager
COMPANY: Food and Drug Administration
FAX: 301-827-2075
RE: **NDA 20-985**
[redacted] **Cream, 0.5%**
(fluorouracil cream)
PAGES: 5 pgs

NOTE – !!
My question was #2 –
They added #1 & 3 VL

Confidential: For Your Eyes Only

Dear Vickey-

Per your voice mail message to Jim Thompson on September 29, 2000, attached for the Division's review are the following documents referencing the above referenced NDA.

1. *Package Insert Pg. 1: Change from* [redacted] *to "methyl methacrylate/glycol dimethacrylate crosspolymer".*
2. *Package Insert Pg. 8: Delete* [redacted] *Change "Collegeville, PA 19426 USA" to "Berwyn, PA 19312, USA".*
3. *Copy of letter from Cosmetic, Toiletry, and Fragrance Association (CTFA) regarding the change in the International Nomenclature Cosmetic Ingredient (ICNC) name for the microsponge.*

If you have any questions, please feel free to contact me at 484-595-2775.

Kind regards,

Alicia Cabrelli

WITHHOLD 2 PAGE (S)

Draft

Labeling

DERMIK LABORATORIES, INC.

1050 WESTLAKES DRIVE
BERWYN, PA 19312
484-595-2700

October 17, 2000

Jonathan Wilkin, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products (HFD-540)
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

AMENDMENT
BL

NDA No. 20-985

TRADENAME Cream, 0.5%
(fluorouracil cream)

Amendment to a Pending Application
Response to FDA Request for Information

Dear Dr. Wilkin:

Reference is made to the telephone conversation on September 29, 2000 between DDDDP Project Manager Ms. Victoria Lutwak and Dermik's Mr. James Thompson, requesting the following information with reference to fluorouracil cream 0.5%.

1. *Package Insert Pg. 1: Change from _____ " to "methyl methacrylate/glycol dimethacrylate crosspolymer". (see attached)*

2. *Package Insert Pg. 8: Delete _____ Change "Collegeville, PA 19426 USA" to "Berwyn, PA 19312, USA". (see attached)*

3. *Copy of letter from Cosmetic, Toiletry, and Fragrance Association (CTFA) regarding the change in the International Nomenclature Cosmetic Ingredient (ICNC) name for the microsponge. (see attached)*

Thank you for your attention. Please contact me at 484-595-2795 if you have any questions.

Sincerely,

James P. Thompson

James P. Thompson
Regulatory Manager
Worldwide Regulatory Affairs

Encl.

DERMIK LABORATORIES, INC.

650 WESTLAKES DRIVE
BERWYN, PA 19312
484-595-2700

NDA ORIG AMENDMENT

October 23, 2000

BL
Faxed

Jonathan Wilkin, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products (HFD-540)
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

NDA No. 20-985
TRADENAME Cream, 0.5%
(fluorouracil cream)

SPONSOR DRAFT LABELING

Dear Dr. Wilkin:

Reference is made to Dermik's response to the Division's draft labeling sent via facsimile on Monday, October 16, 2000 and electronically on Tuesday, October 17, 2000 from DDDDP Project Manager, Vickey Lutwak. Please be advised that the following documents containing Dermik's comments and proposals concerning the labeling proposed by DDDDP were forwarded electronically to Ms. Lutwak on Friday, October 20, 2000.

The following documents are enclosed:

1. *5-FU-rationale3.doc (The location reference in the Draft-102000-withrevisionmarks for each of the proposed changes and the reasons for the change are listed.)*
2. *Draft-102000-withrevisionmarks.doc*
3. *Draft-102000-clean.doc*
4. *Revised data- nda20985packageinsert-DATA for bar charts. (For 1st three bar graphs in package insert -Page 4, Lines 97-114)*

Thank you for your attention. Please contact me at 484-595-2795 if you have any questions.

Sincerely,

James P. Thompson

James P. Thompson
Regulatory Manager
Worldwide Regulatory Affairs

ORIGINAL

BEST POSSIBLE COPY

Encl.

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

1050 Westlakes Drive
Berwyn, PA 19312

Alicia Cabrelli
Regulatory Analyst

TEL. ++ 484-595-2775
FAX: ++ 484-595-2785

FAX TRANSMISSION

DATE & TIME: 10/24/00 11:12 AM
TO: Vickey Lutwak, Project Manager
COMPANY: Food and Drug Administration
FAX: 301-827-2075
RE: **NDA 20-985**
TRADENAME 0.5% fluorouracil cream
PAGES: 5

Confidential: For Your Eyes Only

Dear Vickey-

Per our previous telephone discussions, attached is the document referencing the following commitments:

1. Phase IV
   - Chemistry and Clinical
2. Official Submission of Tradename

If you have any questions, please feel free to contact me at 484-595-2775 or Jim at 484-595-2795.

Kind regards,

Alicia Cabrelli
Regulatory Analyst

APPEARS THIS WAY
ON ORIGINAL

DERMIK LABORATORIES, INC.

1050 WESTLAKES DRIVE
BERWYN, PA 19312
484-595-2700

October 24, 2000

BEST POSSIBLE COPY

Jonathan Wilkin, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products (HFD-540)
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

NDA No. 20-985
fluorouracil Topical Cream, 0.5%

Amendment to a Pending Application
Response to FDA Request for Information
Proposed Tradenames

Dear Dr. Wilkin:

Reference is made to recent telephone conversations representatives of Dermik Laboratories, Inc. had with representatives of the FDA's Division of Dermatological and Dental Drug Products (DDDDP) concerning commitments Dermik was requested to make in this New Drug Application. As a result of these conversations, Dermik commits to the following:

Dermik will not hold or store the bulk fluorouracil drug product for more than ——— from the time of manufacture to the time of packaging.

Dermik will not ——————— drug product without the submission and approval of a supplemental application describing the ——— procedure.

Reference is also made to an October 13, 2000 facsimile transmission from DDDDP Project Manager, Ms. Vickey Lutwak, recommending that Dermik commit to a Phase IV study to assess post-treatment safety and efficacy of our fluorouracil Topical Cream 0.5% product.

As recommended by DDDDP, Dermik commits to a Phase IV study or studies that, together with the patients already treated with our fluorouracil Topical Cream product in controlled clinical trials, will enable Dermik to reach the number of patients treated for actinic keratosis of the face and/or scalp as recommended in the ICH E1A safety guidance. In the study or studies, Dermik will also address the additional safety and efficacy issues delineated in the referenced facsimile (common skin areas not previously treated, recurrence, re-treatment, eye irritation, etc.)

The study protocol or protocols will be submitted to the Agency for review prior to the conduct of said study or studies to assure that the study or studies will address the concerns of the Agency with regard to the use

of the product for the treatment of actinic keratosis. Dermik will initiate the study or studies within one year following the approval of our application. The study or studies will be completed no later than three years after it's (their) initiation, and the results submitted to the Agency within one year after completion.

In addition to these commitments, Dermik is formally submitting the following new tradenames we are proposing for our fluorouracil Topical Cream product:

1. Carac 2. ———————

These names are the same as those submitted verbally to Ms. Vicky Lutwak on October 17, 2000.

If you have any questions concerning our commitments or our proposed product name, please contact us at 484-595-2795.

Thank you for your continuing cooperation.

Sincerely,

James P. Thompson

James P. Thompson
Regulatory Manager
Worldwide Regulatory Affairs

Encl.

APPEARS THIS WAY
ON ORIGINAL

BEST POSSIBLE COPY

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, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICATION INFORMATION

NAME OF APPLICANT Dermik Laboratories, Inc.	DATE OF SUBMISSION October 24, 2000
TELEPHONE NO. *(Include Area Code)* 484-595-2795	FACSIMILE (FAX) Number *(Include Area Code)* 484-595-2785
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 1050 Westlakes Drive Berwyn, PA 19132	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION topical fluorouracil

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)* (fluorouracil cream)	PROPRIETARY NAME *(trade name)* IF ANY N/A
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)* 5-fluoro-2,4(1H,3H)-pyrimidinedione	CODE NAME *(If any)* DL-6025

DOSAGE FORM: Topical Cream	STRENGTHS: 0.5%	ROUTE OF ADMINISTRATION: Topical

(PROPOSED) INDICATION(S) FOR USE: Topical Treatment of actinic keratosis

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:

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

REASON FOR SUBMISSION: Sponsor's Phase IV Commitment and submission of Tradename

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

NUMBER OF VOLUMES SUBMITTED	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

	This application contains the following items: (*Check all that apply*)
	1. Index
	2. Labeling *(check one)* ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50 (d)(1); 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g., 21 CFR 314.50 (e)(2)(i); 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50 (d)(2); 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50 (d)(3); 21 CFR 601.2)
	7. Clinical Microbiology (e.g., 21 CFR 314.50 (d)(4))
	8. Clinical data section (e.g., 21 CFR 314.50 (d)(5); 21 CFR 601.2)
	9. Safety update report (e.g., 21 CFR 314.50 (d)(5)(vi)(b); 21 CFR 601.2)
	10. Statistical section (e.g., 21 CFR 314.50 (d)(6); 21 CFR 601.2)
	11. Case report tabulations (e.g., 21 CFR 314.50 (f)(1); 21 CFR 601.2)
	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b)(2) or (j)(2)(A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (k)(3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. Financial Information (21 CFR Part 54)
X	20. OTHER *(Specify) Sponsor's Phase IV Commitments and submission of Tradename*

CERTIFICATION

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

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
James P. Thompson	James P. Thompson, Manager Worldwide Regulatory Affairs	October 24, 2000

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
1050 Westlakes Drive Berwyn, PA 19312	484-595-2795

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

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

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.

DERMIK LABORATORIES, INC.

1050 WESTLAKES DRIVE
BERWYN, PA 19312
484-595-2700

NDA ORIG AMENDMENT

October 25, 2000

Jonathan Wilkin, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products (HFD-540)
9201 Corporate Boulevard
Building No. 2, Second Floor, Room N115
Rockville, MD 20850

BL

NDA No. 20-985
TRADENAME Cream, 0.5%
(fluorouracil cream)

SPONSOR DRAFT LABELING

Dear Dr. Wilkin:

Reference is made to a teleconference on October 24, 2000 with representatives of the FDA's Division of Dermatological and Dental Drug Products and Dermik Laboratories, Inc.

Please be advised that the following document contains Dermik's comments and proposals concerning the label discussions that were held on October 24, 2000.

The following document is enclosed:

1. *Draft2-102400-withrevisionmarks.doc*

Thank you for your attention. Please contact me at 484-595-2795 if you have any questions.

Sincerely,

James P. Thompson

James P. Thompson
Regulatory Manager
Worldwide Regulatory Affairs

Encl.

ORIGINAL