

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 20-743**

**ENVIRONMENTAL ASSESSMENT AND/OR FONSI**

ENVIRONMENTAL ASSESSMENT  
AND  
FINDING OF NO SIGNIFICANT IMPACT  
FOR

Noritate<sup>®</sup> Cream  
metronidazole cream

1%

NDA 20-743

FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH  
DIVISION OF DERMATOLOGIC AND DENTAL DRUG  
PRODUCTS

(HFD-540)

FINDING OF NO SIGNIFICANT IMPACT

[NDA 20-743]

Noritate® Cream, 1%

metronidazole cream, 1%

The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impact of their actions. FDA is required under NEPA to consider the environmental impact of approving certain drug product applications as an integral part of its regulatory process.

The Food and Drug Administration, Center for Drug Evaluation and Research has carefully considered the potential environmental impact of this action and has concluded that this action will not have a significant effect on the quality of the human environment and that an environmental impact statement therefore will not be prepared.

In support of their new drug application for Noritate Cream, Dermik Laboratories, Inc. has prepared an environmental assessment in accordance with 21 CFR 25.31a(a) which evaluates the potential environmental impacts of the manufacture, use and disposal of the product.

Noritate is a synthetic drug which is administered as a cream in the treatment of rosacea including inflammatory papules, pustules, and erythema. The drug substance will be manufactured by The finished drug product will be used in hospitals, clinics and/or by patients in their homes.

Disposal of the drug may result from out of specification lots, discarding of unused or expired product, and user disposal of empty or partly used product and packaging. Returned or out-of-specification drug substance and rejected or returned drug product will be disposed of at a licensed facility. At U.S. hospitals and clinics, empty or partially empty packages will be disposed according to hospital/clinic regulations. From home use, empty or partially empty containers will typically be disposed of by a community's solid waste management system which may include landfills, incineration and recycling, while minimal quantities of unused drug may be disposed of in the sewer system.

The Center for Drug Evaluation and Research has concluded that the product can be manufactured, used and disposed of without any expected adverse environmental effects. Precautions taken at the sites of manufacture of the bulk product and its final formulation are expected to minimize occupational exposures and environmental release. Adverse effects are not anticipated upon endangered or threatened species or upon property listed in or eligible for listing in the National Register of Historic Places.

2/3/97

DATE

Janet G. Higgins

PREPARED BY

Janet G. Higgins

Review Chemist, HFD-540/830

Division of New Drug Chemistry III

2/1/97

DATE

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Division of New Drug Chemistry III

2/24/97

DATE

Nancy B. Sager

CONCURRED

Nancy B. Sager

Team Leader

Center for Drug Evaluation and Research

Attachments: Environmental Assessment  
Material Safety Data Sheet

cc:

Original NDA 20-743/through Cintron ✓  
HFD-540/Higgins  
HFD-540/De Camp  
HFD-540/Cintron  
HFD-004/FONSI File [NDA 20-743]  
HFD-004/Docket File  
HFD-019/FOI COPY

**ENVIRONMENTAL ASSESSMENT  
NON-CONFIDENTIAL (FOI) VERSION**

- 1.0 DATE December 16, 1996
- 2.0 NAME OF APPLICANT Dermik Laboratories, Inc.
- 3.0 ADDRESS 500 Arcola Road  
P.O. Box 1200  
Collegeville, PA 19426-0107

4.0 DESCRIPTION OF PROPOSED ACTION

a. Requested Approval

Dermik Laboratories, Inc. (Dermik) has filed a New Drug Application (NDA) pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Noritate® (Metronidazole) 1% Cream, 30 grams. This product will be packaged in aluminum #1170 tubes, with internal epoxy coating, and white polypropylene caps. An environmental assessment has been submitted pursuant to 21 CFR § 25.31a(a). Approval is requested to manufacture, package, and market Noritate (Metronidazole) 1% Cream under NDA 20-743.

b. Need for Action

This NDA seeks approval to market a prescription strength 1% metronidazole cream product for use as an antibacterial/antiprotozoal agent, specifically as a topical agent in the treatment of inflammatory papules, pustules, and erythema of rosacea. Metronidazole cream has been widely available by prescription as a topical gel for the treatment of rosacea and has been applied topically to the skin as a 1% cream. The Noritate (metronidazole) 1% Cream drug product will not be administered at higher dosage levels, for longer duration, or for different indications than are currently approved.

The availability of a 1% metronidazole topical cream product is not expected to significantly increase the exposure level of metronidazole. The 1% metronidazole product is intended for consumers who already use or are likely to use metronidazole topical cream for the treatment of rosacea.

c. Production Locations

Noritate (metronidazole) 1% Cream will be manufactured, labeled, packaged, and tested in accordance with NDA 20-743. The active ingredient, metronidazole USP, will be obtained from Farchemia S.R.L. The drug substance will be manufactured at the following location:

No intermediates used to manufacture the drug substance are considered proprietary. Please refer to Drug Master Files (DMFs) and for a description of the facility and the drug substance manufacturing process. A copy of an authorization letter from is included in Attachment 1. A compliance certification statement for the drug substance manufacturing facility is provided in Attachment 2.

The final dosage form of the product, a topical cream, will be manufactured and packaged at the following location:

The facility is located in the heart of the island of Montreal, specifically in the center of the Villeray/Saint-Michel/Parc Extension district, the Villeray sector. Residential areas dominate the Villeray sector, but the industrial sector is well represented. Industrial buildings, located along the metropolitan highway and the CP railway, are mostly manufacturing plants, namely the garment industry, warehouses, repair shops, and factories. The facility is located in an industrial sector situated north of Jarry Park. This industrial area stretches from north to south, bounded respectively by metropolitan highway and by Jarry Street, and from east to west, bounded by the CP railway and de l'Esplanade Avenue. The light industrial zoning allows industrial activities that create only minimal nuisance to the environment.

A compliance certification statement for the drug product manufacturing facility is provided in Attachment 2.

**19<sup>TH</sup>**  
EDITION

# Remington: Practice of

**ALFONSO R GENNARO**

*Chairman of the Editorial Board  
and Editor*

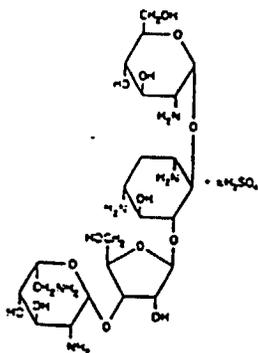
# The Science and Pharmacy

1995

MACK PUBLISHING COMPANY  
Easton, Pennsylvania 18042

### Paromomycin Sulfate

D-Streptamine, O-2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)-O-  
{O-2,6-diamino-2,6-dideoxy-β-L-idopyranosyl-1(1→3)-β-D-  
ribofuranosyl-(1→5)}-2-deoxy, sulfate (salt); Humatin  
(Parke-Davis)



[1263-89-4]; [7542-37-2]; 59-04-1 (paramomycin)  
 $C_{23}H_{42}N_8O_{14} \cdot H_2SO_4$ ; the sulfate of an antibiotic substance or substances  
produced by the growth of *Streptomyces rimosus* var *paramomycinus*,  
or a mixture of two or more such salts. Potency: equivalent to not less  
than 675 μg of paramomycin ( $C_{23}H_{42}N_8O_{14}$ ) per mg, calculated on the  
anhydrous basis.

Preparation—Paromomycin is isolated from fermentation broths by  
ion-exchange adsorption.

Description—Off-white to light-yellow, amorphous powder; odorless  
or practically so; very hygroscopic.

Solubility—1 g in <1 mL water; >10,000 mL alcohol, chloroform or  
ether.

Uses—Effective against most clinically significant gram-negative bacte-  
ria, especially various species of *Shigella* and *Salmonella* and strains of *E*  
*coli*. It is not effective against *Ps aeruginosa*. Among the gram-  
positive organisms, only staphylococci are sufficiently sensitive to be of  
clinical significance. It has been used to treat gastroenteritis or bacterial  
dysentery caused by these organisms, but resistance develops rapidly, the  
relapse rate is high and other antibiotics are more successful. It also has  
been used to reduce the bacterial content of the intestine prior to surgery  
on the bowel or to rid the bowel of nitrogen-forming bacteria in patients  
with hepatic coma.

Its principal and approved use (US) is in the treatment of asymptomatic  
intestinal amebiasis, for which it is an alternative drug. It alters the  
ecology of the intestinal flora in such a way that growth of intestinal  
amebas is discouraged and it also helps to prevent secondary infections  
that may follow or facilitate amebic invasion of the intestinal walls. It is of  
no value in treating hepatic or other extraintestinal abscesses. It also is  
used to treat infections caused by *Disentaria fragilis*. It is an obso-  
lete drug for the treatment of tapeworm infestations.

It often causes gastrointestinal hypermotility, nausea, diarrhea and  
abdominal cramps, which generally appear on the 2nd or 3rd day of treat-  
ment and when the daily dose exceeds 2 g. Occasionally, the drug may  
cause headache, vertigo, vomiting, abdominal pain or skin rash.  
Overgrowth of enteric staphylococci and other pathogenic bacteria rarely  
occurs, but may if treatment is prolonged. Malabsorption syndromes  
have not been reported. There is mutual cross-resistance to kanamycin  
and neomycin, and often to streptomycin. Although it is absorbed poorly  
from the gut, there is potential nephrotoxicity, especially in the presence  
of renal disease.

Dose (base equivalent)—Oral, for intestinal amebiasis and *Disen-*  
*teramoeba* infections, adult and children, 25 to 35 mg/kg a day, in 3  
divided doses with meals, for 5 to 10 days; for hepatic coma, adults, 4 g a  
day in divided doses for 5 or 6 days.

Dosage Form (base equivalent)—Capsules: 250 mg.

## Miscellaneous Antiprotozoal Drugs

Among the protozoal infections that are endemic to the US  
are trichomoniasis, amebiasis, giardiasis and malaria. Other  
protozoal infections, uncommon in the US, nevertheless con-  
stitute serious public health and agricultural problems within  
the possessions and elsewhere. The amebicides and antima-  
larials are useful in the treatment of a number of other proto-  
zoal infections. The antimalarials and amebicides have been  
treated in separate sections above. Consequently, the drugs  
listed below are a miscellaneous group of compounds.

Amodiaquine Hydrochloride—RPS-17, page 1217.

Antimony Potassium Tartrate—page 1338.

### Atovaquone

Mepron (Burroughs Wellcome)

Uses—An analog of ubiquinone with antiprotozoal activity against *Pneu-*  
*mocystis carinii*, *Plasmodium* spp and *Toxoplasma gondii*. Its mecha-  
nism of action is not fully elucidated but antiprotozoal activity may be  
explained by an ability to inhibit selectively mitochondrial electron trans-  
port that results in inhibition of *de novo* pyrimidine synthesis.

It is highly lipophilic with low aqueous solubility. Bioavailability is  
increased significantly with food, but especially by fat. It has a half-life of  
2.9 days and is believed to be excreted in the bile and to undergo enterohep-  
atic cycling with almost all of the drug eliminated in the feces. It is  
highly protein bound (>99.9%).

It is indicated for acute oral treatment of mild to moderate *Pneumocys-*  
*tis carinii* pneumonia (PCP) in patients who are intolerant to  
trimethoprim-sulfamethoxazole. It has not been evaluated adequately as a  
chronic suppressive agent to prevent PCP in patients at high risk for it.

Adverse effects in one study of 203 patients have included rash (23%),  
nausea (21%), diarrhea (19%), headache (16%), vomiting (14%), fever  
(14%), insomnia (10%), asthenia (8%), pruritus (5%), oral monilial (5%),  
abdominal pain (4%), constipation (3%) and dizziness (3%).

Dose—Adult, 750 mg administered with food 3 times a day for 21 days.

Dosage Form—Tablets: 250 mg.

Eflornithine Hydrochloride—see RPS-18, page 1231.

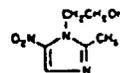
Iodoquinol—page 1324.

Meglumine Antimoniate—see RPS-18, page 1231.

Melarsoprol—see RPS-18, page 1231.

### Metronidazole

1*H*-Imidazole-1-ethanol, 2-methyl-5-nitro-,  
Flagyl (Searle); (Various Mfrs)



2-Methyl-5-nitroimidazole-1-ethanol [443-48-1]  $C_5H_8N_2O_3$  (171.16).

Preparation—2-Methyl-5-nitroimidazole is condensed with ethylene  
chlorohydrin by heating with a large excess of the chlorohydrin. After  
removing the surplus chlorohydrin, the residue is extracted with water and  
the extract is alkalized and extracted with chloroform. Evaporation of  
the chloroform yields crude metronidazole which is recrystallized from  
ethyl acetate. US Pat 2,944,061.

Description—White to pale-yellow, crystals or crystalline powder;  
odorless; stable in air, but darkens on exposure to light; melts between  
159° and 163°;  $pK_a$  2.62.

Solubility—Sparingly soluble in water, alcohol or chloroform; slightly  
soluble in ether.

Uses—Bactericidal to anaerobic and microaerophilic microorganisms,  
including *Bacteroides*, *Clostridium* species, *Endolimax nana*, *Ent-*  
*amoeba histolytica*, *Fusobacterium ruminantium*, *Gardnerella vaginalis*,  
*Giardia lamblia*, *Peptococcus*, *Peptostreptococcus* and *Trichomonas*  
*vaginalis*. These organisms reduce the nitro group and generate metabo-  
lites that inhibit DNA synthesis. It long has been the drug of choice for  
the treatment of trichomoniasis and more recently in combination with  
iodoquinol for the treatment of symptomatic amebiasis (except in brain).  
Because it is absorbed well orally, concentrations in the lower bowel  
sometimes are not high enough to eradicate amebas, so that it is combined

Noritate 1% Cream  
Dermik Laboratories, Inc.  
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**ATTACHMENT 6**  
**Material Safety Data Sheets**



Material Safety Data Sheet  
According to 91/155 EC

Page 2/4

Printing date 03.03.95

Reviewed on 03.03.95

Trade name: metronidazole

(Contd. of page 1)

- Measures for environmental protection:  
Do not allow to enter the ground/soil.
- Inform respective authorities in case product reaches water or sewage system.
- Measures for cleaning/collecting:  
Ensure adequate ventilation.  
Collect mechanically.  
Dispose of the material collected according to regulations.

**7 Handling and storage**

- Handling
- Information for safe handling:  
Thorough dedusting.  
Ensure good ventilation/exhaustion at the workplace.
- Information about protection against explosions and fires:  
Keep breathing equipment ready.
- Storage
- Requirements to be met by storerooms and containers:  
Store in cool location.
- Information about storage in one common storage facility:  
Do not store together with incompatible materials (see Section 10)
- Further information about storage conditions:  
Keep container tightly sealed.  
Protect from the effects of light.

**8 Exposure controls and personal protection**

- Components with limit values that require monitoring at the workplace:
- | CAS No.       | Designation of material | % | Type | Value | Unit |
|---------------|-------------------------|---|------|-------|------|
| Not required. |                         |   |      |       |      |
- Personal protective equipment
  - General protective and hygienic measures  
Keep away from foodstuffs, beverages and food.  
Wash hands during breaks and at the end of the work.  
Avoid contact with the eyes and skin.  
Do not eat or drink while working.
  - Breathing equipment:  
In case of brief exposure or low pollution use breathing filter apparatus. In case of intensive or longer exposure use breathing apparatus that is independent of circulating air.
  - Protection of hands: Protective gloves.
  - Eye protection: Safety glasses

**9 Physical and chemical properties:**

- Form: Crystalline
  - Colour: Cream coloured
  - Odour: Characteristic
  - Change in condition
- |                                   | Value/Range                 | Unit | Method |
|-----------------------------------|-----------------------------|------|--------|
| - Melting point/Melting range:    | 159-163                     | ° C  |        |
| - Boiling point/Boiling range:    | Not determined              |      |        |
| - Flash point:                    | Not applicable              |      |        |
| - Inflammability (solid, gaseous) | Product is not inflammable. |      |        |

(Contd. on page 3)

GB

**Material Safety Data Sheet**  
According to 91/155 EC

Printing date 03.03.95

Reviewed on 03.03.95

<b>Trade name: metronidazole</b>			
(Contd. of page 2)			
- Danger of explosion:	Product is not explosive.		
- Critical values for explosion:			
- Lower:	20 g/m <sup>3</sup>		
- Density	Not determined		
- Solubility in / Miscibility with			
- Water:	at 20 ° C	10 g/l	
- Organic solvents:	Soluble in many organic solvents		
<b>10 Stability and reactivity</b>			
- Thermal decomposition / conditions to be avoided: No decomposition if used according to specifications.			
- Dangerous reactions Reacts with acids, alkalis and oxidizing agents			
- Dangerous products of decomposition: Poisonous gases/vapours			
<b>11 Toxicological information</b>			
- Acute toxicity:			
- LD/LC50 values that are relevant for classification:			
<u>Components</u>	<u>Type</u>	<u>Value</u>	<u>Species</u>
metronidazole	oral	3000 mg/kg	rat
-	ipr	2980 mg/kg	mus
-	scu	3640 mg/kg	mus
- Primary irritant effect:			
- on the skin: No irritant effect.			
- on the eye: No irritant effect.			
- Sensitization: No sensitizing effect known.			
- Additional toxicological information:			
Product is suspected to cause birth defects.			
<b>12 Ecological information:</b>			
- General notes:			
Not known to be hazardous to water. The product has not yet been evaluated by the commission for the evaluation of materials hazardous to water. Until the commission has reached its verdict, the product is evaluated as hazardous to water (WKG 2) in accordance with the recommendations of the VCI (self-evaluation concept).			
<b>13 Disposal considerations</b>			
- Product:			
- Recommendation Must not be disposed of together with household garbage. Do not allow product to reach sewage system.			
- Uncleaned packagings:			
- Recommendation: Disposal must be made according to official regulations.			

Material Safety Data Sheet  
According to 91/155 EC

Page 4/4

Printing date 03.03.95

Reviewed on 03.03.95

Trade name: metronidazole
<b>14 Transport information</b> - Transport/Additional information: Not dangerous according to the above specifications.
<b>15 Regulatory information</b> - Designation according to EC guidelines: The product has been classified and labelled in accordance with EC Directives / Ordinance on Hazardous Materials (GefStoffV) - Code letter and hazard designation of product: Xn Harmful - Risk phrases: 20/21/22 Harmful by inhalation, in contact with skin and if swallowed. 33 Danger of cumulative effects. - Safety phrases: 26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
<b>16 Other information:</b> These data are based on our present knowledge. However, they shall not constitute a guarantee for any specific product features and shall not establish a legally valid contractual relationship. - Department issuing data specification sheet: FARCHEMIA SRL - Contact: Product Safety Department

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INFORMATION FOR OTHER INGREDIENTS IS CONSIDERED CONFIDENTIAL.

Noritate 1% Cream  
Dermik Laboratories, Inc.  
NDA 20-743

ATTACHMENT 7

Expected Introduction Concentration (EIC) Calculation  
and Demonstration of Tier 0 Circumstances

**EXPECTED INTRODUCTORY CONCENTRATION (EIC)  
CALCULATION FOR NORITATE (metronidazole) 1% CREAM  
AND DEMONSTRATION OF TIER 0 CIRCUMSTANCES**

In accordance with Section III.D.6.e of the "Guidance for Industry for the Submission of an Environmental Assessment in Human Drug Applications and Supplements," the Expected Introduction Concentration (EIC) entering into the aquatic environment from patient use has been calculated assuming all drug substance produced is used, evenly distributed throughout the U. S. per day, and no metabolism or depletion mechanisms exist. The EIC is calculated as follows:

$$\text{EIC - Aquatic (ppm)} = A \times B \times C \times D$$

where

A	=	kg/yr production <sup>1</sup>
B	=	1/liters per day entering POTWs <sup>2</sup>
C	=	year/365 days
D	=	10 <sup>6</sup> mg/kg (conversion factor)

- <sup>1</sup> Estimated fifth year production of metronidazole for use in the Noritate 1% Cream product is 126 kg.
- <sup>2</sup> 1.115 x 10<sup>11</sup> liters per day entering publicly owned treatment works, Source: 1992 Needs Survey, Report to Congress, September 1993, EPA 832-R-93-002.

The calculated EIC for the aquatic environment is 0.000003 ppm (0.003 parts per billion (ppb)).

In accordance with Section III.D.7.c of the "Guidance for Industry for the Submission of an Environmental Assessment in Human Drug Applications and Supplements," environmental assessment items 7, 8, 9, 10, 11, and 15 will normally not be needed for drugs whose maximum expected environmental concentration (EEC or EIC whichever is greater) is less than 1 ppb (i.e., Tier 0 conditions). Therefore, since the EIC is less than 1 ppb, Tier 0 conditions are met for the aquatic compartment, and Sections 7, 8, 9, 10, 11, and 15 have been omitted from this environmental assessment.

The EIC for drug substance disposal from production has not been calculated since all pharmaceutical waste associated with production is at a foreign facility (see Attachment 2 for compliance certification).

Noritate 1% Cream  
Dermik Laboratories, Inc.  
NDA 20-743

**ATTACHMENT 8**

**Curriculum Vitae**

## CURRICULUM VITAE

Kenneth M. Feld, Ph.D.

Director

### EDUCATION:

Ph.D., Pharmaceutical Chemistry, The University of Michigan, Ann Arbor, Michigan, 1980.

M.S., Pharmaceutical Chemistry, The University of Michigan, Ann Arbor, Michigan, 1978.

B.S., Biology, State University of New York at Binghamton, Binghamton, New York, 1974.

### EXPERIENCE:

1995 - Present	Director, Product Development and Technical Operations, Dermik Laboratories, Inc. (RPR Company)
1994 - 1995	Senior Director, Product Development Bio-Pharm Pharmaceuticals Services
1993 - 1994	Team Director, Affinity Pharmaceuticals, Inc.
1992 - 1993	Assoc., Vice President, Product Development, Apollon, Inc.
1990 - 1992	Director, Pharmaceutical Technology & Engineering, Rhone-Poulenc Rorer Pharmaceutical Corp.
1986 - 1990	Department Director, Pharmaceuticals, Rorer Pharmaceutical Corp.
1985 - 1986	Section Manager, Pharmaceuticals, Rorer Pharmaceutical Corp.
1983 - 1985	Group Leader, Pharmaceuticals, Rorer Pharmaceutical Corp.
1980 - 1983	Senior Scientist, Pharmaceuticals & Pharmaceutical Technology, CIBA-Geigy, Corp.

## PUBLICATIONS:

S.P. Li, M.G. Karth, K. M. Feld, L. C. DiPaolo, C. M. Pendharkar, R. O. Williams, "Drug Dev. and Ind. Pharm.," 21 (5), 571-590 (1995).

S.P. Li, K. M. Feld, C. R. Kowarski, "Drug Dev. and Ind. Pharm." 20(7), 1121-1145 (1994).

S.P. Li, C. M. Pendharkar, G. N.J. Mehta, M. G. Karth, K. M. Feld, "Drug. Dev. and Ind. Pharm.," 19(19), 2519-2537 (1993).

P-C Sheen, P. J. Sabol, G. J. Alcorn, K. M. Feld, "Drug Dev. and Ind. Pharm.," 18(8), 851-860 (1992).

S. P. Li, K. M. Feld, C. R. Kowarski, "Drug Dev. and Ind. Pharm.," 17(12), 1655-1683 (1991).

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J. C. Liu, J. R. Feldkamp, J. L. White, S. L. Hem, N. Otsuka, D. F. Conroy, C. M. Pendharkar, K. M. Feld, R. J. Harwood and W. M. Grim, "Drug Dev. and Ind. Pharm." 13(12), 2087-2110 (1987).

K. M., Feld, W. I. Higuchi and C. C. Su, "J. Pharm. Sci.," 71, 182 (1982).

K. M. Feld and W. I. Hgiguchi, "J. Pharm. Sci." 70 , 723 (1981).

A. M. Molokhia, A. F. Hofmann, W. I. Higuchi, M. Tuchinda, K. M. Feld, S. Prokongpan and R. G. Danzinger, "J. Pharm. Sci.," 66, 1101 (1977)

A. M. Molokhia, K. M. Feld, M. Tuchinda, W. I. Higuchi and A. F. Hofmann, "Gastro.," 69, 849 (1975).

## PATENTS:

J. R. Luber, K. M. Feld, R. J. Harwood, W. M. Grim, "Process for the Preparation of a Viscosity Stable Antacid Suspension."

**PROFESSIONAL AFFILIATIONS:**

PMA: The Pharmaceutical Industry Visiting Scientist Program

Adjunct Professor, Temple University, College of Pharmacy

American Association of Pharmaceutical Scientists

1994 Arden House Program Chairperson

The Controlled Release Society

**SPECIAL TRAINING PROGRAMS:**

1990 - 1992            "Quality and Productivity Improvement for Competitiveness",  
Rhone-Poulenc Rorer Pharmaceutical Corp. .

1991                    "International Deming User's Group Conference"

1986                    "PMA: Management Development Seminar," Columbia  
University Graduate School of Business

1984                    "Managing for Productivity," Rorer Pharmaceutical Corp.

1983                    "Kepner - Tregoe Decision Analysis, " Ciba-Geigy Corp.

## CURRICULUM VITAE

Brian Lipsitz, CHMM, P.G.

### Education:

MS Ocean Sciences/Coastal Zone Management, Nova University, 1987.

BS Geosciences, Pennsylvania State University, 1981.

### Experience:

#### 1993-present Environmental Project Manager

Integrated Environmental Services Lafayette Hill, PA

Responsible for environmental compliance projects in the manufacturing sector, primarily for the pharmaceutical manufacturing and biotechnology sectors. Completed numerous assignments involving the preparation of environmental assessments for New Drug Applications to the FDA, and assisted facilities in obtaining necessary permits and approvals, completing required plans and documentation, and maintaining overall environmental compliance with applicable federal, state, and local environmental regulations. Project activities have required interaction with multi-disciplinary groups within the pharmaceutical industry including plant engineering, solid dose & liquids manufacturing, R&D, regulatory affairs, planning, purchasing, and contract operations.

Environmental projects have included conducting multi-media environmental compliance audits, developing pollution prevention plans, environmental baseline and closure assessments, and preparing permit applications and compliance documentation for manufacturing facilities in the areas of solid and hazardous waste, air quality, wastewater, storm water, SARA Title III, aboveground and underground storage tanks, OSHA, and transportation of hazardous materials. Project management responsibilities have included proposal and budget development, subcontractor & vendor selection and oversight, technical report writing and editing, and interaction with federal, state, and local regulatory agencies. Considerable experience has been gained in preparing operating plans, permits, and technical reports within federal regulatory agency guidelines and protocols. Extensive projects have been completed for pharmaceutical manufacturing facilities to analyze and improve operations while maintaining compliance with applicable regulations.

#### 1989-1993 Project Manager

Burns and Roe Environmental Services King of Prussia, PA and Oradell, NJ

Managed a variety of environmental projects for manufacturing facilities involving compliance determinations, permitting, and process evaluation to support engineering design projects. Environmental projects included multi-media facility compliance audits and regulatory reviews, environmental permitting, phase I and II soil and groundwater site assessments, underground storage tank evaluations, and regulatory reviews under CERCLA, RCRA, TOSCA, and state hazardous waste and water programs. Other responsibilities included technical writing and editing, regulatory agency interfacing, project scheduling and budgets, proposal preparation, financial reporting, manpower selection, and cost allocation.

**1988-1989**      **Project Manager**  
NUS Corporation Wayne, PA

Performed preliminary assessments and site inspections of potential uncontrolled hazardous waste sites as a subcontractor to the EPA under the CERCLA and RCRA programs. Responsibilities included interfacing with EPA site investigation officers, preparing work plans, health and safety plans, and conducting risk assessment studies according to the Hazard Ranking System model. Analyzed on-site treatment, storage, and disposal methodologies, solid waste management units, and audited site operations and environmental characteristics at active and inactive industrial facilities.

**1985-1987**      **Chemist and Geologist**  
Spectrum Laboratories Ft Lauderdale, FL

Implemented a groundwater sampling and analysis program to identify the nature and extent of pollutants at a municipal landfill, industrial manufacturing facilities, and wastewater treatment plants. Performed water quality analyses and analytical testing on soil, sludge, wastewater, and groundwater samples.

**1983-1984**      **Geologist**  
University of Texas/Bureau of Economic Geology Austin, TX

Processed, examined, and catalogued geologic core samples to support a feasibility study for the U. S. Department of Energy in order to evaluate potential locations for an underground nuclear waste repository.

**1981-1982**      **Geologist**  
Exxon Minerals Company Cookeville, TN

Managed the field sampling program of a geochemical exploration project to identify ore-bearing, massive sulfide deposits in Central Arkansas. Responsibilities included geologic mapping, stream sediment and soil sampling, geophysical surveying, watershed evaluation, and oversight of field personnel.

## **Professional Associations, Training, & Publications:**

**Certifications**    · Certified Hazardous Material Manager  
                         · Registered Professional Geologist - Pennsylvania & Tennessee  
                         · OSHA 40-Hour Hazardous Waste Operations

**Training**            · Pennsylvania Hazardous Waste Regulations  
                         · OSHA Hazard Communication Program Training

**Associations**    · Academy of Certified Hazardous Materials Managers  
                         · American Geophysical Union  
                         · Philadelphia Geological Society

**Publications**    *Streamlining The Process*, B. Lipsitz, Plants, Sites, and Parks, May 1994.

Attachment VII

whb  
12/15/96  
727

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee  
Attention: Daniel L. Boring, Ph.D., Chair, (HFD-530)

From: Division of Dermatological and Dental Drug Products;  
HFD-540

Attention: Janet G. Higgins Phone 827-2068

Date: 12/13/96

Subject: Request for Assessment of a Trademark for a Proposed Drug Product

Proposed Trademark: Noritrate® Cream NDA# 20-743  
Company Name: Dermik Laboratories, Inc.

Established name, including dosage form: Metronidazole Cream, 1%

Other trademarks by the same firm for companion products: \_\_\_\_\_

Indications for Use (may be a summary if proposed statement is lengthy): for the topical treatment of rosacea including inflammatory papules, pustules, and erythema

Initial comments from the submitter: (concerns, observations, etc.)  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Note: Meetings of the committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Consult #727 (HFD-540)

NORITATE

metronidazole cream 1%

The Committee noted the following look-alike/sound-alike conflict with NORITATE: NORLUTATE. The Committee feels this conflict has a low potential for confusion. There were no misleading aspects found in this proposed proprietary name.

The Committee has no reason to find the proposed proprietary name unacceptable.

D. Bering 2/5/97, Chair  
CDER Labeling and Nomenclature Committee