CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-400

ENVIRONMENTAL ASSESSMENT AND/OR FONSI

ENVIRONMENTAL ASSESSMENT

AND

FINDING OF NO SIGNIFICANT IMPACT

FOR

Avita (Tretinoin) Gel, 0.025%

NDA 20-400

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

DIVISION HFD-540

FINDING OF NO SIGNIFICANT IMPACT

NDA 20-400

Avita (Tretinoin) Gel

The Food and Drug Administration (FDA) recognizes the National Environmental Policy Act of 1969 (NEPA) as the national charter for protection, restoration, and enhancement of the environment. NEPA establishes policy, sets goals (section 101), and provides procedures (section 102) for carrying out the policy.

Environmental information is to be available to the public and the decisionmaker before decisions are made about actions that may significantly affect the quality of the human environment; FDA actions are to be supported by accurate scientific analyses; and environmental documents are to concentrate on timely and significant issues, not to amass needless detail.

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, Penederm Incorporated has prepared an abbreviated environmental assessment 21 CFR 25.31a which evaluates the potential environmental impacts of the manufacture and use of Avita, Tretinoin Gel, 0.025%. The drug is indicated for topical treatment of acne vulgaris. The point sources of manufacture of the drug substance is at
the signed certification of
compliance is provided. The finished product is manufactured at the
the compliance statement is included.

The Center for Drug Evaluation and Research has concluded that the product can be manufactured and used 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.

5/24/96 /S/

DATE PREPARED BY
Nahid Mokhtari-Rejali, Ph.D.
Chemist, HFD-830

7/22/96 /S/

DATE DIVISION CONCURRENCE
Wilson De Camp, Ph.D.
Team Leader, Chemistry
HFD-830

DATE Approved
Environmental Assessment Officer
Office of the Center Director
Center for Drug Evaluation and Research

Attachments: Environmental Assessment
Material Safety Data Sheet for tretinoin

CC: Original NDA 20-404/HFD-540
Division File(s)

FONSI File _____/HFD-540
N. Sager/HFD-102
Docket File 20-404/HFD-540
FOIA Copy HFD-019 (HOLD UNTIL APPROVED)

NDA #20-400: AVITA™ (TRETINOIN) GEL 0.025%
ENVIRONMENTAL ASSESSMENT
ABBREVIATED FORMAT 25.31a(b)(3)
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NDA #20-400: AVITA™ (TRETINOIN) GEL 0.025%
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NDA #20-400: AVITA™ (TRETINOIN) GEL 0.025%
ENVIRONMENTAL ASSESSMENT
ABBREVIATED FORMAT 25.31a(b)(3)

1. DATE

Revised November 20, 1996

2. NAME OF APPLICANT

Penederm Incorporated

3. ADDRESS

320 Lakeside Drive
Suite A
Foster City, CA 94404

4. DESCRIPTION OF PROPOSED ACTION

A. REQUESTED APPROVAL

Penederm requests the approval of Avita (tretinoin) Gel 0.025%, topical formulation for the treatment of acne vulgaris. The proposed action encompasses the manufacture of the drug substance, tretinoin, and the finished product manufacturing, testing, packaging, and use of the topical product.

The product is packaged in 2-gram, 20-gram, and 45-gram epoxy/phenolic-lined aluminum tubes with a blinded end and a polypropylene screw cap. All tubes are then packaged in cartons.

B. NEED FOR ACTION

Tretinoin is a keratolytic agent known to be effective topically in the treatment of acne vulgaris. According to 25.31a(b)(3), the information is arranged in the abbreviated format.

In the course of evaluating the efficacy of retinoic acid and the emolliency of potential formulation excipients, the sponsor identified the gel formulation presented here, Avita Gel 0.025%, which has subsequently been evaluated and found to be therapeutically equivalent to the marketed Retin-A® gel product, and superior to vehicle control in the treatment of acne vulgaris. The formulation is intended to be used for the topical treatment of acne vulgaris. In addition, the formulation appears to cause less irritation than the currently marketed Retin-A formulation.

Tretinoin, also known as vitamin A acid, is a derivative of retinol (vitamin A) and is an endogenous substance in humans. Tretinoin and retinol are necessary for the growth and differentiation of epithelial tissue and skin. After dietary consumption, retinol and retinol esters are stored in the liver and other tissues, and are released to maintain endogenous plasma levels of tretinoin and retinol. Conditions associated with tretinoin and retinol deficiencies can present as keratinization and drying of the epidermis, increased incidence of respiratory infections, diarrhea, degeneration of the testes, night blindness, nerve lesions, and thick, cancellous bone.

The indication proposed is the treatment of acne vulgaris with topical tretinoin. Kligman first demonstrated that topically applied tretinoin is clinically effective in the treatment of acne vulgaris. Tretinoin acts through a reduction in keratinization, an increase in basal cell proliferation, and an increase in the desquamation of the epidermis.

Acne is a dermal disease. It has many causes and manifestations, but its primary presentations are papules, pustules, and nodules. The initial presentation of acne is as a noninflammatory hyperkeratinization in the follicular duct also known as comedo formation. Comedones result from failure to exfoliate normally the keratinized epidermal cells lining the follicular canal. Tretinoin is a highly effective chemical commonly used in acne treatment because it serves many physiological functions at both cellular and tissue levels.

Although tretinoin and retinol do not circulate similarly, they do enter cells by related receptors. Tretinoin and retinol appear to exert their biological effects intracellularly through binding to cytosol receptors. Three of the most commonly recognized cytosolic retinoid-binding proteins are: cellular retinol binding protein (CRBP), cellular retinoic-acid binding protein (CRABP), and retinoic-acid receptor (RAR).

The net effect of dermal application of tretinoin is the normalization of altered epithelial structures, produced in part by a marked increase in epithelial proliferation and desquamation. The return to a more organized tissue is initiated at both a cellular and ultrastructural level. At the cellular level, hyperproliferation of keratinizing cells in the basal layer leads to a thickening of the granular layer. The rapid increase in epithelial tissue also leads to a thinning or compaction of the stratum corneum in which the horny cells become flatter and more uniform. Coupled with the physical changes of the stratum corneum are intercellular changes.

Increased vasculature in the epidermis generally accompanies topical tretinoin treatments as does intercellular edema and spongiosis. The increase in intercellular fluid increases the distance between cells causing cell membranes to push apart. In the edemic tissue surrounding the follicle, polymorphonuclear leukocytes collect, invade the follicular lining, and form pools between the horny kernel and the encapsulating membrane. The massing of polymorphonuclear leukocytes around the horn-filled follicle brings about a discharging of the comedone through the weakening of its anchorage. Tretinoin not only has the effect of expulsing open comedones, but of changing closed comedones to open ones that are subsequently discharged.

The cells of the stratum corneum treated with tretinoin do not reach terminal differentiation. Treated cells generally contain substantial lipid droplets of large numbers. A marked diminution of tonofilaments is thought to lead to the decrease in cellular cohesion. Also, it has been shown that tretinoin suppresses proteolysis of certain keratins critical in cornification of cells in the horny layer. There are reports of the inhibition of the keratin-binding substance, filaggrin *in vitro* by tretinoin. All of these factors combine to make a stratum corneum with poor cohesion that is easily sloughed.

Topical treatment with tretinoin produces a reorganized epidermis, intercellular edema, and a compacted but unstable stratum corneum. The fragility of the stratum corneum created by tretinoin application allows for sloughing off of this epithelium, the expulsion of both open and closed comedones, and the prevention of microcomedone formation.

C. LOCATION OF PRODUCTION

The drug substance is manufactured by:

The drug substance is supplied by:

Complete manufacturing, processing, and packaging of Avita Gel 0.025% is done by:

is responsible for component receipt testing, compounding, in-process testing, packaging, and bulk and finished product release testing.

Raw material vendor qualification testing, finished product release to market, and stability evaluations are the responsibility of:

Penederm Incorporated
320 Lakeside Drive
Suite A
Foster City, CA 94404

D. LOCATION OF USE AND DISPOSAL OF DRUG PRODUCT

Avita Gel 0.025% will be used by individuals throughout the United States. Other than the trace metabolites that result from topical application of the product, the small amount of material remaining unused by the patient is anticipated to be disposed of nationally as solid wastes and handled in accordance with local conventions (landfill, incineration).

Waste generated from the production of Avita Gel 0.025% will be disposed of in accordance with local, state, and federal requirements. utilizes the resources of licensed, bonded, and certified waste disposal firms for both hazardous and nonhazardous disposal.

Rejected, returned, or expired drug product, rejected raw materials, and scrap from packaging lines will be disposed of by incineration by the hazardous waste disposal contractor identified in Attachment 1 of the Confidential Environmental Assessment.

General nonhazardous plant refuse including waste paper and corrugated will be disposed of by landfill by the nonhazardous waste disposal contractor identified in Attachment 1 of the Confidential Environmental Assessment.

Water for cleaning and cooling used in the manufacturing of the drug product are discharged into the sewage treatment system. The permits for this purpose are identified in Attachment 2 of the Confidential Environmental Assessment.

E. ENVIRONMENTAL SETTING OF DPT LABORATORIES

is located approximately two miles from the center of the City of San Antonio in a light manufacturing/ industrial area at has been at this location since 1953 and has conscientiously observed all environmental conditions for this type of facility. Additional information about the facility is provided in Section 6., Introduction of Substances to the Environment.

5. LIST OF CHEMICAL SUBSTANCES THAT ARE SUBJECT TO THE PROPOSED ACTION

All relevant chemical information on the drug substance is summarized on the following page. As mentioned previously in this document, tretinoin drug substance has been available on the market for over ten years. The MSDS for tretinoin is provided as Attachment 1.

A. DRUG SUBSTANCE:

Names:

Established Chemical Name: (Generic Name)	Tretinoin
Alternative Names: (Synonyms)	Retinoic acid All-*trans*-retinoic acid Vitamin A acid
Code Designation:	CAS Registry #302-79-4

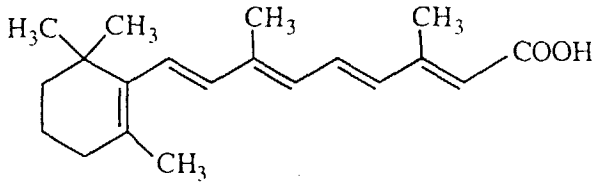
Physical and Chemical Characteristics:

Appearance and Physical Form: Yellow powder

Empirical Formula: $C_{20}H_{28}O_2$

Molecular Weight: 300.44

Structural Formula:



For complete information regarding the physical and chemical characteristics of the drug substance, reference is made to Drug Master File, DMF A letter of authorization to reference this DMF is provided in Volume 1.1.1 of NDA #20-400.

Manufacturer:

The drug substance is manufactured by:

The drug substance is supplied by:

B. DRUG PRODUCT:

Avita Gel 0.025% appears as a translucent, yellow gel with smooth texture and ethanolic odor.

A list of the other ingredients used in this dosage form is provided below. These ingredients are commonly used in the pharmaceutical and/or cosmetic industry.

- Ethanol, 95%, denatured
- Polyolprepolymer-2
- Hydroxypropyl cellulose, NF
- Butylated hydroxytoluene, NF or FCC

6. INTRODUCTION OF SUBSTANCES TO THE ENVIRONMENT

Solid waste accumulated during cleaning and rejected goods at the manufacturing site are disposed of via government-permitted techniques. Returned goods received by Penederm are disposed of via government-permitted techniques.

A. MANUFACTURING

Drug Substance:

The drug substance, tretinoin, is manufactured by:

The drug substance is supplied by:

is in compliance with all applicable environmental regulations in Germany.

Drug Product:

Complete manufacturing, processing, and packaging of Avita Gel 0.025% is done by:

is responsible for component receipt testing, compounding, in-process testing, packaging, and bulk and finished product release testing.

is registered with the EPA and the local Emergency Planning Commission regarding the storage of chemicals located at this site. location is listed as: Latitude 20°, 26 minutes, 45 seconds; Longitude 98°, 28 minutes, 43 seconds.

Since effective controls are utilized in the receipt, storage, and use of these substances, probable impact on the environment would be minimal. Controls exercised in the handling of these substances are as follows:

- Covered loading dock for receipt of substances
- Environmentally-controlled and covered warehouse storage areas
- Localized dust collection units for sampling, weighing, and dispersing ingredients
- Handling of ingredients is conducted in appropriately controlled manufacturing areas.
- Preparation of batch is conducted in environmentally-controlled and GMP-controlled areas.

Waste generated from the production of Avita Gel 0.025% will be disposed of in accordance with local, state, and federal requirements. utilizes the resources of licensed, bonded, and certified waste disposal firms for both hazardous and nonhazardous disposal.

It is anticipated that preparation of Avita Gel 0.025% will have no significant impact on any existing waste streams.

Wastewater Permit:

The San Antonio Water System, Wastewater Quality Division is responsible for assuring that San Antonio complies with EPA and state requirements for wastewater discharge, stormwater runoff, and other applicable functions. They conduct quarterly, random wastewater sampling to monitor plant discharge as well as semi-annual inspections of the facility for compliance. In order to continue to discharge into the wastewater system, the agency also requires self-monitoring, semi-annual tests to assure effluent meets requirements. This permit does not have a fixed expiration date but is continually monitored for compliance. Permit information is reviewed and updated by city personnel on a semi-annual basis. The current permit was issued in 1992.

Texas Natural Resource Conservation Commission (TNRCC):

This agency is responsible for enforcing EPA regulations, both state and federal, regarding the generation, storage, and disposition of both nonhazardous and hazardous waste. Under the regulation of this authority, generates, stores, and disposes of various categories of liquid and solid waste, manifests shipments when required, and submits annual summary reports on waste generated. is currently registered as a small quantity generator and meets all the provisions for this category. This permit does not expire as long as the generator's conduct does not significantly change. When wastewater streams are added or modified, the authority issues a revised permit to cover those activities. The current permit was issued in 1993.

EPA and RCRA ID Number:

This particular identification number is issued by the TNRCC and is used in all pertinent state and federal reporting activities regarding various generation, storage, and disposition of both hazardous and nonhazardous waste. This number remains the same unless there is a change in ownership, location, or other significant reason.

Air Quality:

has been exempted from requiring an air pollution license by the City of San Antonio, San Antonio Metropolitan Health District. This agency is charged with maintaining air quality standards in the city limits of San Antonio. This exemption will be in effect as long as continues at their current low level of emissions.

Safety:

Operating procedures are established to minimize exposure to chemicals. Health and environmental monitoring is performed as required. manufacturing employees participate in group and individual health and safety training programs. Training regarding the proper operation of both manufacturing equipment and material-handling equipment is conducted. Monthly reviews of employee safety records are conducted and recorded in a formalized report. Routine blood profile monitoring is conducted for manufacturing, technical, and other personnel who might come in contact with products manufactured at the facility. Annual blood profiles are compared to baselines previously established by qualified medical personnel.

Appropriate particulate monitoring of environmental air is conducted by in-house personnel for evaluation of bioburden and by a contract industrial hygienist for determination of airborne exposure levels. Additionally, determination of decibel ratings of different pieces of the manufacturing equipment is made to identify any potential areas where hearing protection is required.

Employees routinely receive documented training in the safe and proper handling of all chemicals used in the department and have Material Safety Data Sheets available for timely reference. Prior to manufacturing Avita Gel 0.025%, compounders review the safety precautions outlined in the section provided in the Compounding Module. Personal safety protective equipment available includes surgical latex gloves when handling chemical components of the drug product; safety glasses/goggles worn during the entire manufacturing process; and personal respirators when handling chemicals which are prone to generation of dust and/or exposure to organic vapors. Tyvek disposable coveralls, shoe coverings, and head protection are also available when required.

is currently operating in compliance with all applicable emission requirements (including operational) at local, state, and federal levels and the additional production of Avita Gel 0.025% should not have any appreciable effect on ability to continue to comply with environmental emission/discharge requirements. Attached is General Compliance Statement which attests to this.

Emergency Response Plan:

In the event of a minor release, the Emergency Response Team is activated and the area is evacuated. Plant personnel who are trained in emergency response will re-enter the area wearing proper protective clothing and respiratory protection to take remedial action. Emergency equipment immediately available includes: Hazmat carts, spill control kits, personal protective equipment, respirators, rescue and escape air, and first aid supplies.

In the event of a serious release or an escalation of an existing situation, the external emergency plan will take effect with plant evacuation and mobilization of the Regional Hazmat Team, Fire Department, and Hospital/Emergency Services.

All material generated during a clean-up will be treated as hazardous and dealt with according to federal, state, and local regulations.

The maximum possible amounts of tretinoin from manufacturing that could possibly end up in wastewater are provided in Attachment 4 of the Confidential Environmental Assessment.

Raw material vendor qualification testing, finished product release to market, and stability evaluations are the responsibility of:

Penederm Incorporated
320 Lakeside Drive
Suite A
Foster City, CA 94404

Penederm is located on flat terrain in an urban area.

B. COMPLIANCE STATEMENTS

Compliance statements for each of the three facilities and Penederm Incorporated) are provided on the following pages.

PENEDERM INC.
attn. Bhaskar Chaudhuri, Ph. D.
320 Lakeside Drive
Foster City, CA 94404

USA

Letter of Compliance

Dear Dr. Chaudhuri,

we hereby certify that the facilities in for the manufacturing of TRETINOIN are

1. in compliance with all local and national environmental laws;
2. in compliance with, or are on an enforceable schedule to be in compliance with, all emission requirements set forth in all permits; and
3. that approval and the subsequent increase in production at the facility is not expected to affect compliance with current emission requirements or compliance with environmental laws.

Sincerly,

Preiskorn Schwarz

September 20, 1994

GENERAL COMPLIANCE STATEMENT

states that it is in compliance with, or on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the production of TRETINOIN GEL at its facilities at as well as emission requirements set forth in applicable federal, state and local statutes and regulations applicable to the production of TRETINOIN GEL at its facilities located at

Michael J. Bordovsky
Vice President
Manufacturing Operations

Terrance Clifford
Manufacturing Manager

COMPLIANCE STATEMENT

Penederm Incorporated states that it is in compliance with, or on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees, and administrative orders applicable to the storage, handling, and disposition of Avita Gel 0.025% at its facilities in Foster City, California as well as emission requirements set forth in applicable federal, state, and local statutes and regulations applicable to the production of Avita Gel 0.025% at its facilities in Foster City, California.

John Quigley, PhD
Senior Vice President
Research and Development

11/20/96
Date

7. FATE OF EMITTED SUBSTANCES

These items are ordinarily not required according to 25.31a(b)(3). The toxicologic and pharmacologic properties of the drug substance indicates that the amount entering the environment is considerably lower than the amount required to elicit adverse effects in microorganisms or any other species.

*8. ENVIRONMENTAL EFFECTS OF RELEASED SUBSTANCES

*9. USE OF RESOURCES AND ENERGY

*10. MITIGATION MEASURES

*11. ALTERNATIVES TO THE PROPOSED ACTION

* These items are ordinarily not required according to 25.31a(b)(3), as indicated in the "Guidance for Industry For the Submission of an Environmental Assessment in Human Drug Applications and Supplements," CDER, November 1995, CMC 6, pages 7 and A-1.

12. LIST OF PREPARERS

This document was prepared by:

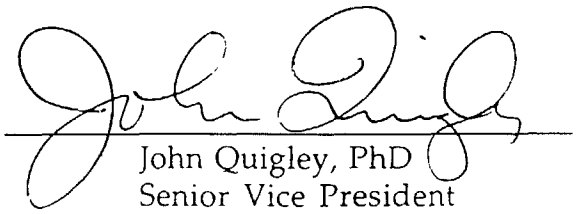
Sui Yuen Eddie Hou, PhD
Research Scientist, Formulations and Product Development

Bhaskar Chaudhuri, PhD
Executive Director, Pharmaceutical Sciences

Barry Calvarese, MS
Executive Director, Clinical/Regulatory Affairs

13. CERTIFICATION

The undersigned official certifies that the information presented is true, accurate, and complete to the best of his knowledge.



John Quigley, PhD
Senior Vice President
Research and Development

11/20/96
Date

ATTACHMENT 1

Material Safety Data Sheet

Original Date: 01/04/1994
Revision Date: 03/12/1996

SECTION 1 - PRODUCT INFORMATION

TRETINOIN, USP
Product ID: NVN 684821
Common Chemical Name:
RETINOIC ACID
Synonyms:
ALL-TRANS-RETINOIC ACID, VITAMIN A ACID
Molecular Formula:
C(20)H(28)O(2)

Chemical Family: Vitamin
Molecular Wt.: 300.4

SECTION 2 - INGREDIENTS

Chemical Name:	CAS	Amount
RETINOIC ACID	302-79-4	~ 100.0 %
PEL/TLV NOT ESTABLISHED		

SECTION 3 - PHYSICAL PROPERTIES

Color: Yellow
Form/Appearance: Crystalline Powder
Odor: Odorless

	Typical	Low/High	U.O.M.
Specific Gravity:	NOT AVAILABLE		
Bulk Density:	~ 0.48		G/CC
pH:		6 - 7	SU

	Typical	Low/High	Deg.	@	Pressure
Boiling Pt:	NOT AVAILABLE				
Freezing Pt:		176 - 182	C	1	ATMOSPHERES
Decomp. Tmp:	~ 60		C	1	ATMOSPHERES

Solubility in Water Description: Insoluble
SOLUBLE IN MANY ORGANIC SOLVENTS

SECTION 4 - FIRE AND EXPLOSION DATA

	Typical	Low/High	Deg.	Method
Flash Point:	NOT AVAILABLE			

ATTACHMENT 1 (CONTINUED)

SECTION 4 - FIRE AND EXPLOSION DATA (cont)

	Typical	Low/High	Deg.	Method
Autoignition:	265		C	DIN 51794

Extinguishing Media:
Use water fog, foam or dry chemical extinguishing media.
Fire Fighting Procedures:
Firefighters should be equipped with self-contained breathing apparatus and turn out gear.
Unusual Hazards:
Adequate ventilation and cleanup must be maintained to minimize dust accumulation. May form explosive dust-air mixture.

SECTION 5 - HEALTH EFFECTS

Routes of entry for solids and liquids include eye and skin contact, ingestion and inhalation. Routes of entry for gases include inhalation and eye contact. Skin contact may be a route of entry for liquified gases.

Toxicology Test Data:
Rat, Oral LD50 - < 2 G/KG
Moderately Toxic
Health Effects Testing -
Irritating
Mouse, Oral LD50 - 5,500 (30%)
Slightly Toxic
Rabbit, Dermal LD50 - > 2500(50%) MG/KG
Slightly Toxic
Rabbit, Primary Skin Irritation - 50 % AQ.SOL.
Nonirritating
Rabbit, Primary Skin Irritation - 50 % AQ.SOL.
Nonirritating
Rabbit, Eye Irritation -
Nonirritating
Mouse, IP Dominant Lethal Assay - @104 MG/KG
Not mutagenic
Mouse, Acute Intraperitoneal LD50 - 550 (APPROX) MG/KG
Moderately Toxic
Rat, Acute Intraperitoneal LD50 - 350 (APPROX) MG/KG
Very Toxic
Rat, Dermal LD50 - > 2000 MG/KG
Slightly Toxic
Acute Overexposure Effects:
Contact can cause irritation to the eyes, skin, and mucous membranes. Prolonged skin contact may result in dermatitis or blistering. Material can be skin absorbed.
Ingestion of excessive amounts of vitamin A may result in headaches, nausea, blurred vision, and decreased appetite.
Chronic Overexposure Effects:
Chronic overexposure to vitamin A is associated with low red blood count, low leukocyte count, joint/bone pain, fatigue, depression, skin rash, and liver & spleen abnormalities. Some cases of hyper-vitaminosis A, have resulted in bone changes and CNS effects. Animal

ATTACHMENT 1 (CONTINUED)

SECTION 5 - HEALTH EFFECTS (cont)

studies have shown that vitamin A is teratogenic in several species.

First Aid Procedures - Skin:
Wash affected areas with soap and water. Remove and launder contaminated clothing before reuse. If irritation develops, get medical attention.

First Aid Procedures - Eyes:
Immediately rinse eyes with running water for 15 minutes. Get immediate medical attention.

First Aid Procedures - Ingestion:
If swallowed, dilute with water and immediately induce vomiting. Never give fluids or induce vomiting if the victim is unconscious or having convulsions. Get immediate medical attention.

First Aid Procedures - Inhalation:
Move to fresh air. Aid in breathing, if necessary, and get immediate medical attention.

First Aid Procedures - Notes to Physicians:
None known.

First Aid Procedures - Aggravated Medical Conditions:
No data is available which addresses medical conditions that are generally recognized as being aggravated by exposure to this product. Please refer to Section 5 (Effects of Overexposure) for effects observed in animals.

First Aid Procedures - Special Precautions:
None

Special Precautions: Under no circumstances should the product come in contact with the skin of pregnant women or be inhaled by them.

SECTION 6 - REACTIVITY DATA

Stability Data:
Stable

Incompatability:
Acids.
Oxidizers

Conditions/Hazards to Avoid:
Avoid dust cloud formation.

Hazardous Decomposition/Polymerization:
Hazardous decomposition products: None known.
Polymerization: Does not occur.

Corrosive Properties:
Not Corrosive.

Oxidizer Properties:
Not an oxidizer

SECTION 7 - PERSONAL PROTECTION

Clothing:
Gloves, coveralls, apron, boots as necessary to minimize contact.

Eyes:
Chemical Goggles

Respiration:
If dusts are generated, wear an approved dust respirator.

ATTACHMENT 1 (CONTINUED)

SECTION 7 - PERSONAL PROTECTION (cont)

Ventilation:
Use local exhaust to control dusts.
Explosion Proofing:
None required.
Other Personal Protection Data:
Eyewash fountains and safety showers must be easily accessible.

SECTION 8 - SPILL-LEAK/ENVIRONMENTAL

General:
Spills should be contained, solidified and placed in suitable containers for disposal in a licensed facility. This material is not regulated by RCRA or CERCLA ("Superfund"). Wear appropriate respiratory protection and protective clothing and provide adequate ventilation during clean-up.
Waste Disposal:
Incinerate or bury in a licensed facility. Do not discharge into waterways or sewer systems without proper authority.
Container Disposal:
Dispose of in a licensed facility. Recommend crushing or other means to prevent unauthorized reuse.
Environmental Toxicity Test Data:
Ready Biodegradability: Modified MITI - > 70 PERCENT
Readily Biodegradable
Inhibition of activated sludge; LC20 - 300 MG/L
No Inhibition

SECTION 9 - STORAGE AND HANDLING

General:
Store at moderate temperatures in tight, light-resistant containers.

SECTION 10 - REGULATORY INFORMATION

TSCA Inventory Status
Listed on Inventory: YES
Product Grades: USP: Y NF: FCC:

This product is hazardous or contains components which are hazardous according to the OSHA Hazard Communication Standard.

SECTION 11 - TRANSPORTATION INFORMATION

DOT Proper Shipping Name:
NONE
DOT Technical Name:
NONE
DOT Primary Hazard Class:
NONE
DOT Secondary Hazard Class:
NONE
DOT Label Required:
NONE
DOT Placard Required:
NONE

ATTACHMENT 1 (CONTINUED)

SECTION 11 - TRANSPORTATION INFORMATION (cont)

DOT Poison Constituent:
NONE
BASF Commodity Codes: 453 453 UN/NA Code: N/A .. E/R Guide:

Bill of Lading Description:
FOOD, DRUGS OR MEDICINE, NOIBN

	CLASS:	P. G.	SHIPPING NAME:
IATA:	NONE	N/A	NONE
IMO:	NONE	N/A	NONE
TDG:	NONE	N/A	NONE

"IMPORTANT: WHILE THE DESCRIPTIONS, DESIGNS, DATA AND INFORMATION CONTAINED HEREIN ARE PRESENTED IN GOOD FAITH AND BELIEVED TO BE ACCURATE, IT IS PROVIDED FOR YOUR GUIDANCE ONLY. BECAUSE MANY FACTORS MAY AFFECT PROCESSING OR APPLICATION/USE, WE RECOMMEND THAT YOU MAKE TESTS TO DETERMINE THE SUITABILITY OF A PRODUCT FOR YOUR PARTICULAR PURPOSE PRIOR TO USE. NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ARE MADE REGARDING PRODUCTS DESCRIBED OR DESIGNS, DATA OR INFORMATION SET FORTH, OR THAT THE PRODUCTS, DESIGNS, DATA OR INFORMATION MAY BE USED WITHOUT INFRINGING THE INTELLECTUAL

END OF DATA SHEET