# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER: NDA 20773

# ENVIRONMENTAL ASSESSMENT AND/OR FONSI

SEP 1 1 1997

# ENVIRONMENTAL ASSESSMENT

# AND

# FINDING OF NO SIGNIFICANT IMPACT

# FOR

## SonoRx®

## (simethicone 0.25% coated cellulose oral suspension)

## NDA 20-773

## FOOD AND DRUG ADMINISTRATION

## CENTER FOR DRUG EVALUATION AND RESEARCH

## DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS (HFD-160)

**FINDING OF NO SIGNIFICANT IMPACT**

**NDA 20-773**

**SonoRx®**

**(simethicone 0.25% coated cellulose oral suspension)**

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 **SonoRx® (simethicone 0.25% coated cellulose oral suspension)**, **Bracco Diagnostics, Inc.** has prepared an environmental assessment in accordance with 21 CFR 25.31a (attached) which evaluates the potential environmental impacts of the manufacture, use and disposal of the product.

SonoRx® is an ultrasound imaging contrast agent which will be administered orally. The drug substance will be manufactured by [redacted] and Bristol Myers Squibb Company. The drug product will manufactured by Westwood Squibb. The finished drug product will be used by trained professionals in hospitals and clinics throughout the United States.

Simethicone coated cellulose may enter the environment from excretion by patients, from disposal of pharmaceutical waste or from emissions from manufacturing sites. The projected environmental introduction concentration from use is less than 1 ppb. CDER has routinely found that concentrations less than 1 ppb have no effect on relevant standard test organism, therefore the applicant has submitted a Tier 0 EA without format items 7, 8, 9, 10 and 11.

Disposal in the United States may result from returned, recalled or expired goods and user disposal of empty or partly used product and packaging. Returned, recalled or expired goods will be sent to a licensed disposal facility. At U.S. hospitals and clinics, empty or partially empty packages will be disposed according to hospital/clinic procedures.

Precautions taken at the sites of manufacture of the bulk product and its final formulation are expected to minimize occupational exposures and environmental release.

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. 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.

9/11/97
DATE

/S/
PREPARED BY
Nancy B. Sager
Team Leader
Environmental Assessment Team
Center for Drug Evaluation and Research

9-11-97
DATE

/S/
CONCURRED
Eric B. Sheinin, Ph.D.
Director, Office of New Drug Chemistry
Center for Drug Evaluation and Research

Attachment: Environmental Assessment

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

1. **DATE:** **September 27, 1996**

2. **NAME:** **Bracco Diagnostics Inc.**

3. **MAILING ADDRESS:** **P.O. Box 5225**
**Princeton, NJ 08543-5225**

4. **DESCRIPTION OF PROPOSED ACTION**

A. Requested Approval

Bracco Diagnostics Inc. is requesting approval for the use of SonoRx® (simethicone 0.25% coated cellulose oral suspension). SonoRx® is an ultrasound imaging contrast agent. SonoRx® is administered orally with a normal dose of 400 mL.

B. Need For Action

SonoRx® is an ultrasound imaging contrast agent that is used for the delineation of anatomy and detection or exclusion of pathology in the upper abdomen including the upper GI tract and the retroperitoneum.

C. Production Locations

1. Drug Substance

Simethicone coated cellulose, the active ingredient in the product which is the subject of the proposed action, is manufactured by the following (two) contract manufacturers:

i.

ii. Bristol-Myers Squibb Company
US Pharmaceutical Group
2400 W. Lloyd Expressway
Evansville, Indiana 47721

2. Drug Product

The final drug product, SonoRx© will be formulated and packaged at the Bristol-Myers Squibb Westwood Squibb Pharmaceuticals Technical Operations facility, 100 Forest Avenue, Buffalo, New York 14213. This facility is located in an urban area and has programs and systems in place to comply with all applicable environmental regulations.

There are no known rare or endangered species inhabiting the area surrounding the facility; there are also no nature preserves or protected areas nearby.

D. Locations of Use

SonoRx® will be used worldwide for the delineation of anatomy and detection or exclusion of pathology in the upper abdomen including the upper GI tract and the retroperitoneum. SonoRx® will be used by trained professionals in hospitals and clinics. It is anticipated that its distribution will be primarily to economically-developed countries, particularly in the United States and Europe.

E. Disposal Sites

1. Drug Substance

Abbott: Please refer to DMF

BMS: Rejected drug substance received in Evansville, Indiana will be disposed of as non-hazardous waste at an approved and permitted landfill in accordance with all federal, state and local regulations. Refer to Confidential Appendix, Section 1 for information on the approved landfill.

2. Drug Product

The product returned to the Bristol-Myers Squibb Company will be received at the Distribution Center located in Mount Vernon, Indiana. This site is the designated pharmaceutical finished product returned goods processing center for the product. has contracted with a third party processor of returned goods, to process the returns of finished pharmaceuticals from direct and indirect customers. Finished product that is expired, damaged, unwanted or unsalable is returned to the from other BMS Distribution Centers or from customers, where it is checked and inventoried pending disposition. Product may be placed back into inventory, sent back to a processing site for further evaluation or directed for disposal according to standard operating procedures. All

returns awaiting final disposition are held in quarantine status within the facility.

Product that is destined for disposal from this site is classified as "non-hazardous" off-specification pharmaceutical. It is appropriately packed by facility personnel and loaded for transport to [ ] incineration facility in [ ] Refer to Confidential Appendix, Section 1 for applicable permit information.

[ ] is the designated pharmaceutical customer returns finished product processing center. Finished product that is expired, damaged, unwanted, or unsalable is returned from customers, processed and accumulated for disposal.

Product from [ ] that is destined for disposal is classified as "non-hazardous" off-specification pharmaceutical. It is appropriately packed by facility personnel and loaded for transport to [ ] waste to energy facility in [ ] Refer to the Confidential Appendix, Section 1 for applicable permit information.

Transportation to the disposal sites is done by an approved carrier. The shipping papers are prepared by site personnel. The disposal sites acknowledge receipt by signing and returning copies of the shipping paper. The disposal facilities confirm in writing when the actual destruction of waste occurred.

APPEARS THIS WAY
ON ORIGINAL

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

## 5. IDENTIFICATION OF SUBSTANCES THAT ARE SUBJECT TO THE PROPOSED ACTION

A. Nomenclature

i. Established Name: Simethicone (0.25%) coated cellulose
ii. Brand/Proprietary Name: SonoRx® (simethicone coated cellulose oral suspension)
iii. Chemical Names: Simethicone (0.25%) coated cellulose

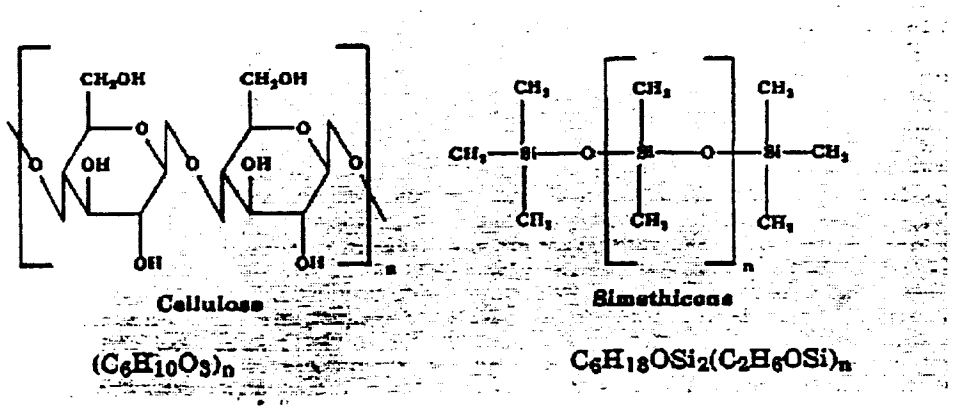
B. Chemical Abstract Service Number: Not available

C. Molecular Formula:

Cellulose: $(C_6H_{10}O_3)_n$
Simethicone: $C_6H_{18}OSi_2(C_2H_6OSi)_n$

D. Molecular Weight: Not applicable

E. Structure:




F. Physical Description: Simethicone coated cellulose is a white of off-white powder.

G. Additives: Not applicable

H. Impurities: No impurities greater than 1 %

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

## 6. INTRODUCTION OF THE SUBSTANCES INTO THE ENVIRONMENT

Introduction of the drug substance and drug product into the environment can occur from the drug substance manufacturing site, the final product manufacturing and packaging facility, the site of intended use by humans, the distribution center and, the disposal of drug product.

A. Substances Expected to be Emitted

For substances expected to be emitted, refer to the Confidential Appendix 2.

B. Controls Exercised

Drug Substance Manufacturing

Abbott: Please refer to DMF

BMS: The manufacturing of the simethicone coated cellulose should not have any adverse impact on the environment. Its introduction into the environment as a result of manufacture is expected to be negligible. Wastes generated consist of wastewater, solid waste and air emissions. Each is described below for the final product manufacturing and packaging in Evansville, Indiana

1. Air Emissions

Air emissions at the Bristol-Myers Squibb Evansville site from the drug substance manufacture are controlled through the use of emission-control equipment, principally wet scrubbers, that are registered by the city of Evansville Environmental Protection Agency (EPA).

2. Liquid Waste

Waste water from the Evansville manufacturing site is discharged into a Publicly Owned Treatment Works (POTW), specifically the city of Evansville's Westside Wastewater Treatment Plant.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

3. Solid Waste

The drug substance(s) are not listed hazardous waste as defined by 40 CFR Section 261. All non-hazardous solid waste generated from the manufacture of the drug substances are collected in appropriate containers and disposed of at an approved and permitted landfill in accordance with all federal, state and local regulations.

The Drug Product Manufacturing and Packaging Facility

The manufacturing of the simethicone coated cellulose suspension should not have any adverse impact on the environment. Its introduction into the environment as a result of manufacture is expected to be negligible. Wastes generated consist of wastewater, solid waste and air emissions. Each is described below for the final product manufacturing and packaging in Buffalo, New York.

1. Liquid Waste

Wastewater will be generated from cleaning of process and packaging equipment i.e. mixing kettle. mixer, hopper, etc. This wastewater will contain small quantities of drug product. The initial rinse of the cleaning process which contains most product residue left on the equipment is captured in a wastewater holding tank where it mixes with other equipment cleaning wastewaters. This waste is sent off-site for wastewater treatment to . The subsequent wastewaters from the cleaning process are discharged to the Buffalo Sewer Authority in accordance with permit # 93-01-BU175.

2. Air Emissions

Dust control equipment will be used to minimize any particulate emissions. The equipment is designed with a control efficiency of 99%.

3. Solid Waste

No hazardous waste will be generated by the manufacturing and packaging processes. Solid waste generated by the manufacturing and packaging processes will be collected and sent to . Other ancillary solid waste generated, such as surplus packaging materials and manufacturing supplies will be landfilled at an approved off-site facility.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

C. Citation of and Statement of Compliance with Applicable Emission Requirements

All necessary actions have been or will be taken so that emissions, discharges and wastes from the production of the simethicone coated cellulose suspension will be in compliance with applicable environmental and occupational health and safety standards and Federal, State, or local regulations and permits.

1. Citations of Applicable Federal, State and Local Regulations

Listed below are citations of applicable Federal, State and local emission requirements and laws:

i. **Federal - United States**

Major environmental statutes with regulations promulgated by the United States Environmental Protection Agency that may impact pharmaceutical manufacturing include:

**Air Quality:** Clean Air Act of 1977 as amended 1990; 42 United States Code (U.S.C.) §§ 7401-7671q; 40 Code of Federal Regulations (C.F.R.) Parts 50-88

**Waste:** Resource Conservation and Recovery Act 1976 as amended by the Hazardous and Solid Waste Act Amendments 1984; 42 U.S.C. §§ 6901-6992; 40 C.F.R. Parts 240-281

**Remediation:** "Superfund," Comprehensive Environmental Response, Compensation and Liability Act of 1980; 42 U.S.C. §§ 9601-9675; 40 C.F.R. Parts 300-311

**Water:** Clean Water Act of 1972; 33 U.S.C. §§ 1251-1387; 33 C.F.R. Parts 320-330; 335-338; 40 C.F.R. Parts 104-140, 230-233, 401-477

**Chemicals:** Emergency Planning and Community Right-to-Know Act of 1986 (Superfund Amendments and Reauthorization Act Title III, SARA Title III) 42 U.S.C. §§ 11001-11050; 40 C.F.R. Parts 350, 355, 370, 372; Pollution Prevention Act of 1990; 42 U.S.C. §§ 13101-13209

**Energy:** Atomic Energy Act of 1954; 42 U.S.C. §§ 2011-2297g-2; 10 C.F.R. Parts 0-171, 760-766, 810-962; Energy Reorganization Act of 1974; 42 U.S.C. §§ 5801-5891; 10 C.F.R. Parts 88, 40.7, 50.7, 70.7, 708; Low-Level Radioactive Waste Policy Act of 1980; 42 U.S.C. §§ 10 C.F.R. Parts 61-62; Regulations implemented by the Atomic Energy Commission

**Occupational Safety & Health:** Occupational Safety and Health Act of 1970; 29 U.S.C. §§ 651-78; 29 C.F.R. Parts 1900-1910

ii. **Buffalo, New York**

State

Solid Waste Management Regulations

-6NYCRR 360, 370, 371, 372, 376

Prevention and Control of Air Contamination and Air Pollution - Permits and Registrations; General Process Emission Sources

-6NYCRR 201, 212

Registration of Petroleum Storage Facilities; Handling and Storage of Petroleum

-6NYCRR 612, 613

Local

Buffalo Sewer Authority Sewer Use Code

iii. **Evansville, Indiana**

State - Indiana

Solid Waste Management Rules
329 IAC Article 2

Solid Waste Management Air Pollution Control Rules
326 IAC Article 2

Permit Review Rules
326 IAC Article 3

Monitoring Requirements Water Pollution Control Rules
327 IAC Article 5



Industrial Wastewater Pretreatment Programs (NPDES)

Indiana Occupational Safety & Health Act (IOSHA)
Tittle 22, Article 8, Chapter 1.1

Local - Evansville

Evansville Ordinance 5.53, Wastewater Discharge Regulations (local sewer ordinance).

2. Emission Permits

Listed in the following section are the emission permits and/or registrations, according to air, liquid and solid waste streams.

Drug Substance Manufacture

Abbott: Please refer to DMF number

BMS:

i. Air Emissions

Control equipment used at the BMS Evansville site for the drug substance processes are registered by the city of Evansville EPA. An annual fee for operation is required under ID#015. The city of Evansville EPA inspects the site at least annually and is responsible for issuing the permits and registrations.

ii. Liquid Waste

The wastewater from the Evansville manufacturing site discharges into a Publically Owned Treatment Works (POTW), specifically the city of Evansville's Westside Wastewater Treatment Plant (NPDES permit number IN0032956). The Evansville plant's industrial pretreatment permit from the city of Evansville is registered under Mead Johnson & Company.

iii. Solid Waste

The non-hazardous solid waste generated from the drug substance manufacture is sent to an approved and permitted landfill. Refer to the Confidential Appendix for a listing of the applicable disposal site(s).

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

Drug Product Manufacture

i. Air Emissions

Control equipment used at the Westwood-Squibb Buffalo site is registerd with the New York State Department of Environmental Conservation. An annual fee is paid to operate emission point ID #00012. Routine inspections are performed by the agency. The Certificates to Operate are valid for a five year time period.

ii. Liquid Waste

The wastewater from the Buffalo site discharges into a POTW specifically the Buffalo Sewer Authority. SPDES permit # NY0028410. The POTW has issued a discharge permit to the Buffalo site, 96-01-BU175.

iii. Solid Waste

The drug product waste, a non-hazardous waste will be sent to _____ to be incinerated. Other ancillary waste such as surplus packaging materials and manufacturing supplies will be landfilled at _____ site in accordance with permit WCD25608.

D. Discussion of the Effect of Approval on Compliance with Current Emission Requirements

The operation for the manufacture of the simethicone coated cellulose suspension does not involve any new construction, thus there will be no impact on land use, water quality or other natural resources from any construction activities.

The manufacturing of the simethicone coated cellulose suspension should not have any adverse impact on the environment. Its introduction into the environment as a result of manufacture is expected to be negligible.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

E. Expected Introduction Concentration

i. Expected Introduction Concentration From Use

The Expected Introduction Concentration (EIC) entering the aquatic environment from patient use is determined as follows:

EIC-Aquatic (ppm) = A x B x C x D

Where

A = kg/year production
B = 1/liter per day entering POTWs*
C = year/365 days
D = $10^6$ mg/kg

* $1.115 \times 10^{11}$ liters per day entering Publicly Owned Treatment Works (POTWs), source: 1992 Needs Survey, Report to Congress, September 1993, EPA 832-R-93-002.

EIC-Aquatic (ppm) = See Confidential Appendix 3

ii. Expected Introduction Concentration from Disposal

An expected introduction concentration for disposal was not calculated because as previously described in Section 4.E.2, the drug product wastes will be disposed of in approved and permitted landfills. Refer to Section 4.E.2 of this environmental assessment for further information on disposal practices.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

## 7. FATE OF EMITTED SUBSTANCES IN THE ENVIRONMENT

Based on the expected introduction concentration, Tier 0 exists and this section is not required.

## 8. ENVIRONMENTAL EFFECTS OF RELEASED SUBSTANCES

Based on the expected introduction concentration, Tier 0 exists and this section is not required.

## 9. USE OF RESOURCES AND ENERGY

Based on the expected introduction concentration, Tier 0 exists and this section is not required.

## 10. MITIGATION MEASURES

Based on the expected introduction concentration, Tier 0 exists and this section is not required.

## 11. ALTERNATIVE TO PROPOSED ACTION

Based on the expected introduction concentration, Tier 0 exists and this section is not required.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

## 12. LIST OF PREPARERS

James Kearney, MS, Environmental Health, University of Cincinnati; BA, Biology, University of Buffalo; Certified Industrial Hygenist; Certified Safety Professional; practicing professional since 1980 with experience in industrial hygiene, safety and environmental protection.

Beth L. Bidstrup, MHS, Industrial Hygiene and Safety, The Johns Hopkins University; BS, Industrial Hygiene and Environmental Toxicology, Clarkson University; Certified Industrial Hygienist, practicing professional since 1986 with experience in industrial hygiene and safety.

Lawrence Callan, MS, Chemistry, Rutgers University; BS, Chemistry, Manhattan College, Director Regulatory Operations, employed in the pharmaceutical industry since 1969 with experience in Quality Control and Regulatory Affairs.

## 13. CERTIFICATION

The undersigned certified that the information presented is true, accurate and complete to the best of the knowledge of Bristol-Myers Squibb and Bracco Diagnostics Inc.

The undersigned official certifies that the environmental assessment summary document (pages 3 193 - 3 206) contain non-confidential information and acknowledges that this information will be made available to the public in accordance with 40 CFR § 1506.6.

Signature Lawrence Callan Date 9/27/96

Lawrence Callan
Director, Regulatory Operations
Bracco Diagnostics Inc.

# ENVIRONMENTAL ASSESSMENT
# SIMETHICONE COATED CELLULOSE SUSPENSION

## 14. REFERENCES


1. Guidance for Industry "For the Submission of an Environmental Assessment in Human Drug Applications and Supplements," Food and Drug Administration Center for Drug Evaluation and Research (CDER), November 1995, CMC 6, pages 1-E1.

2. "Interim Guidance to the Pharmaceutical Industry for Environmental Assessment Compliance Requirements for the FDA." Pharmaceutical Manufacturers Association. version 7, July 1991.

3. "Technical Assistant Document," FDA Environmental Assessment Technical Assistance Handbook NTIS PB 87-175345-, March, 1987.

4. National Environmental Policy Act (NEPA), 42 USC 4332, (1969) 83 Stat. 853.

5. FDA Final Rule for Compliance with National Policy Act: Policy and Procedure, Federal Register 50 FR 16636, 21 CFR 25, April 16, 1985.

**Regarding section 4 of the EA:**

**1. You have failed to address the following information in the EA for public release:**

**1.a. Facility descriptions and adjacent environments for the facility.**

Where found in the Environmental Assessment for SonoRx ™ dated August 12. 1993, the manufacturing facility is over 200 acres in size. The Site is located in an industrial zoned area within the . The operations are 600 to 1,000 feet west of at an elevation approximately fifty (50) feet above the 580 foot mean sea level elevation of the lake. Other than , there are no significant geographic features, such as mountains or rivers, in close proximity to the Area topography is fairly flat, sloping gently east toward Drainage is dominantly to the east-southeast, toward

geology consists of approximately 105 feet of unconsolidated Quaternary Age glacial deposits overlying much older Silurian Dolomite bedrock formations. The glacial deposits consist primarily of silty clay tills, sand and gravel outwash, and lake bottom silt and clay deposits. These materials were deposited during the Wisconsinan Age, which occurred from 75,000 to 7,000 years ago and was the last glaciation period for the region.

The area climate is characterized by warm summers (74 to 94$^0$F) and cold winters (20 to 32$^0$F). Average annual rainfall is 32 inches, and wind directions are primarily from the west and can be highly variable.

**1.b. Disposal locations for the Abbott facility.**

Where found in the Environmental Assessment for SonoRx ™ dated August 12, 1993, the Solid and liquid non-hazardous, pharmaceutical, and hazardous wastes generated during production are collected and shipped off-site to state and federal permitted commercial disposal facilities. These off-site facilities are licensed to treat or dispose of the wastes. does not own or operate any solid waste landfills.

Several of the state and federal permitted off-site disposal, recycling or energy recovery facilities noted in the Environmental Assessment for SonoRx ™ dated August 12, 1993 are no longer contracted by Any wastes generated from the process may be sent to the following facilities:

**Regarding item 6 of the EA:**

**2.b. No discussion of the controls exercised were made for the site.**

Where found in the Environmental Assessment for SonoRx ™ dated August 12, 1993, the manufacturing site has air, water and solid waste control devices and treatment systems. Air pollutants generated from the bulk drug production process are controlled using condensers, particle filters, carbon adsorbers, and scrubbers. Wastewater's are treated on-site in two stages: (1) physical and chemical treatment for pH control and solids removal, followed by (2) anaerobic and aerobic biologic treatment using the activated sludge process. If necessary, additional wastewater treatment may be performed using distillation and stripping equipment to remove certain waste constituents from the process wastewater prior to discharge into the activated sludge process wastewater treatment system. All wastewater is discharged to a Public Owned Treatment Works (POTW), operated by the North Shore Sanitary District, where it is again treated in an aerobic activated sludge wastewater treatment system.

Condensers will be used to control organic vapor emissions during production, with an approximate 90% control efficiency. Additional emission control equipment may be connected to the process equipment to provide emissions control as necessary or desired. Sufficient plant manufacturing and emissions control equipment capacity exists to significantly expand production of this product and maintain compliance with all environmental permits and regulatory requirements. No environmental permit or regulatory constraints are foreseen with the future production plans for this product.



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2.c. **A citation for the site (i.e., list of regulations/laws) of all applicable Federal, State and local emission requirements, including occupational, as well as a statement of compliance with, or being on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the manufacturing operations should be made.**

As stated in the original SonoRx™ Environmental Assessment dated August 12, 1993 in Section 6 (pages 4 and 5), the is subject to environmental laws and regulations promulgated and enforced by the US Environmental Protection Agency, the Environmental Protection Agency, the and the various local ordinances of the city of Some of these regulations include the wastewater Effluent Guidelines and Standards for Pharmaceutical Manufacturing defined in Title 40 of the Code of Federal Regulations (40 CFR) Part 439, the Illinois State Implementation Plan regarding ambient air quality as approved by the US under 40 CFR Part 52, and the Hazardous Waste Regulations defined in 40 CFR. See attached General Environmental Compliance Statement.

2.f. **For the site, the EA failed to state whether approval and the subsequent increase in production at the facility is expected to affect compliance with current emission requirements. This should contain a brief supporting discussion based on the estimated fifth year production volume.**

As stated in Section 6 of the original SonoRx™ Environmental Assessment (dated August 12, 1993), the acceptance of this DMF will have no effect on compliance with environmental permits or limitations. Although fifth year estimates are not available, sufficient plant manufacturing and emissions control equipment capacity exists to significantly expand production of this product and maintain compliance with all environmental permits and regulatory requirements. No environmental permit or regulatory constraints are foreseen with the future production plans for this product.

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ON ORIGINAL

**CHEMICAL AND AGRICULTURAL PRODUCTS DIVISION**

GENERAL ENVIRONMENTAL COMPLIANCE STATEMENT

states that it is in material compliance with, or on an internal or enforceable schedule to be in compliance with, all applicable emission requirements set forth in permits, consent decrees and administrative orders relating to the production of SonoRx bulk drug at its facilities in as well as applicable emission requirements set forth in federal, state and local statutes and regulations relating to such production.

Daniel J. Wozniak
Senior Environmental Coordinator
Chemical and Agricultural Products Division

4/7/97
dated

1. **You have failed to address the following information in the EA for public release:**

   **1.a. Facility descriptions and adjacent environments for the BMS Indiana facility.**

   The Evansville plant is located on a 60-acre site adjacent to the Ohio River, within the city of Evansville in Vanderburgh County. The immediate neighborhood includes a school and residential areas, as well as other industrial and commercial businesses. The upper soil is silty clay.

   There are no known rare or endangered species inhabiting the area surrounding the facility; there are also no nature preserves or protected areas nearby. The site is not within the 100-year flood plain of the Ohio River.

**2.a. You have failed to provide a MSDS for the drug substance. Please provide the information.**

A copy of the MSDS is provided on the following pages.

The information presented herein, while not guaranteed, was prepared by technically knowledgeable personnel and to the best of our knowledge, is true and accurate. It is not intended to be all inclusive and the manner and conditions of use and handling may involve other and additional considerations.

# MATERIAL SAFETY DATA SHEET

| Name (As Used on Labels and Lists) | Note: Blank spaces are not permitted. If any item is not applicable, or no information is available, the space must be marked to indicate that. |
|---|---|
| Sano-X 1200-00 | |

## Section I

| Manufacturer's Name | Emergency Telephone Number |
|---|---|
| Westwood-Squibb Pharmaceuticals | (716) 887-3400 |
| Address (Number, Street, City, State, and ZIP Code) | Telephone Number for Information |
| 100 Forest Avenue | (716) 887-3400 |
| Buffalo, New York 14213 | Date Prepared: 3/93 |
| | Signature of Preparer (optional) |

## Section II – Hazardous Ingredients/Identity Information

| Hazardous Components (Specific Chemical Identity; Common Name(s)) | OSHA PEL | ACGIH TLV | Other Limits Recommended | % (optional) |
|---|---|---|---|---|
| N/Ap | | | | |

## Section III – Physical/Chemical Characteristics

| Boiling Point | N/Av | Specific Gravity (H$_2$O = 1) | 1.0 |
|---|---|---|---|
| Vapor Pressure (mm Hg.) | N/Av | Melting Point | N/Ap |
| Vapor Density (AIR = 1) | N/Av | Evaporation Rate (Butyl Acetate = 1) | N/Ap |

Solubility in Water: Infinite

Appearance and Odor: Orange liquid suspension with orange odor

## Section IV – Fire and Explosion Hazard Data

| Flash Point (Method Used) | Flammable Limits | LEL | UEL |
|---|---|---|---|
| N/Ap | N/Ap | N/Ap | N/Ap |

Extinguishing Media: $CO_2$, powder

Special Fire Fighting Procedures: None

Unusual Fire and Explosion Hazards: None

N/Ap = Not Applicable N/Av = Not Available

| | | | |
|---|---|---|---|
| Explosive | Unstable | | Conditions to Avoid: Extreme heat or freezing. Product will be damaged |
| | Stable | Y | |

Incompatibility (Materials to Avoid): None known

Hazardous Decomposition or Byproducts: None known

| | | | |
|---|---|---|---|
| Hazardous Polymerization | May Occur | | Conditions to Avoid |
| | Will Not Occur | Y | |

## Section VI – Health Hazard Data

Routes of Entry: Inhalation? Skin? Ingestion? Oral

Health Hazards (Acute and Chronic): N/Ap Toxicity study scheduled for 4/93

Carcinogenicity: N/Ap NTP? IARC Monographs? OSHA Regulated?

Signs and Symptoms of Exposure: N/Ap

Medical Conditions Generally Aggravated by Exposure: N/Ap

Emergency and First Aid Procedures: N/Ap

## Section VII – Precautions for Safe Handling and Use

Steps to Be Taken in Case Material is Released or Spilled: Neutralize with weak base

Waste Disposal Method: Follow all Local, State and Federal Regulations

Precautions to Be Taken in Handling and Storing: None

Other Precautions: None

## Section VIII – Control Measures

Respiratory Protection (Specify Type): None required

| | | |
|---|---|---|
| Ventilation | Local Exhaust | Special |
| | Mechanical (General) | Other: General ventilaton sufficient |

Protective Gloves: None required

Eye Protection: Avoid eye contact as with any foreign ma

Other Protective Clothing or Equipment: None

Work/Hygienic Practices: N/Ap

**2.d. No statement respective to the BMS, Indiana site was provided of compliance with, or being on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the manufacturing operations.**

Please see the statement provided on the following page.

February 12, 1997

Mr. L. Callan
Bracco Diagnostics, Inc.
P.O. Box 5225
Princeton, NJ 08543-5225

Dear Mr. Callan:

The Bristol-Myers Squibb Co. Evansville, Indiana facility is in compliance with, or being on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the manufacturing operations of SonoRx® (simethicone coated cellulose suspension).

Sincerely,

John E. Wellemeyer
Facility Manager

JEK-185/bac

cc: J. E. Kearney, BMS, Syracuse

2.d. **No statement respective to the BMS, Westwood site was provided of compliance with, or being on an enforceable schedule to be in compliance with, all emission requirements set forth in permits, consent decrees and administrative orders applicable to the manufacturing operations.**

Please see the statement provided on the following page.

WESTWOOD SQUIBB

100 Forest Avenue Buffalo, NY 14213-1091
(716)887-3400 (800)333-0950

July 31, 1997

Mr. L. Callan
Bracco Diagnostics, Inc.
P.O. Box 5225
Princeton, NJ 08543-5225

Mr. Callan:

The Westwood Squibb, Buffalo, New York facility is in compliance with all emission requirements set forth in permits, consent decrees and administrative orders applicable to the manufacturing operations of SonoRx® (simethicone coated cellulose suspension).

Very truly yours,

James P. Walter
Senior Director, Operations