CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-388

ENVIRONMENTAL ASSESSMENT/FONSI

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information

ENVIRONMENTAL ASSESSMENT

AND

FINDING OF NO SIGNIFICANT IMPACT

FOR

STERILE TALC POWDER

5.0 GRAM PER BOTTLE

NDA 21-388

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DIVISION OF ONCOLOGY DRUG PRODUCT (HFD-150)

FINDING OF NO SIGNIFICANT IMPACT

NDA 21-388

STERILE TALC POWDER

5.O gram per Bottle

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 Sterile Talc Powder, 5.0 g per bottle Bryan Corporation has prepared an environmental assessment submitted in Vol. 2, Part B, Attachment 3.3, pp 445 –455 in accodance with 21 CFR Part 25 which evaluates the potential environmental impacts of the use and disposal from use of the product.

Sterile Talc Powder (5.0 g per bottle) is the same as the drug substance. Talc is very stable natural material with no possible hazardous reaction and no decomposition products. Talc is administered intrapleurally via chest tube for the treatment of malignant pleural effusion.

Talc is contained in a standard 100 mL glass bottle which is closed with a rubber stopper sealed with an aluminum band and blue plastic flip off seal. The bottle or vial is contained in a — pouch. At the time of use, Talc is hydrated with sterile saline. The suspension is instilled into the pleural cavity of patients suffering from malignant pleural effusion by intrapleural injection through a chest tube.

The sponsor plans to market the product in the United States where it will be supplied to physicians for in-hospital use. Hospital pharmacies will receive cases of 10 bottles. The talc instillation will result in a coating o f talc on the pleural surfaces, which has been shown, in post-mortem studies , to remain largely in place during the remainder of the patient's life. It is not systematically absorbed and will not be excreted. The entire contents of the vial are typically used during the application. Each vial is single use.

Since hospitals will typically order small quantities to support their staff physicians needs and bottles can be stored unopened in the hospital pharmacy until physicians request them, few unused bottles will ever be disposed of. Empty bottles, which are glass, can be recycled by the hospitals after use.

The talc in the vial is a solid, in powder form, which is inert and relatively insoluble. For use the talc must be made into a slurry by the addition of sterile saline. The slurry is drawn up into two syringes then instilled in the pleural cavity through a chest tube. After instillation into the pleural cavity, it will remain on the pleural surfaces where it acts as a sclerosing agent and reduces the effusions. It is not systemically absorbed; therefore it will not be excreted. The bulk of the substance will remain in the patients lungs for the length of time that the MPE patient lives.

Unless the vial is broken, very little, if any of the talc will enter the air. Amounts that do become airborne due to breakage of the vial could be spread around due to the powdery nature of the material, but they will ultimately fall to the ground or local surfaces in the area in which the break occurred.

Talc is very sparingly soluble in water. No significant amount will enter the aquatic compartment.

Talc is a naturally occurring chemically inert substance. Any amounts that do become airborne and later settle to the ground will not react with any other substance that they come in contact with.

The talc used will not have any adverse effect on the atmosphere.

The talc used will not have any adverse effect on the aquatic environment. The likelihood of this material reaching the aquatic environment is very small.

The talc used will not have any adverse effect on terrestrial ecosystems.

Water and electricity are used in the mining operations. Trucks at the site are probably diesel-powered. The incremental amounts of resources and energy used at the quarry to supply the talc for Bryan Corporation are not a significant amount of the overall usage.

——— ., where the bottles are filled and packaged uses electricity and water.

— where the product is sterilized will use electricity and a source of gamma irradiation.

Use of the bottles will not require natural resources or energy.
Disposal of used bottles into the recycling stream will entail use of electricity as well as diesel fuel for the trucks used to haul this type of waste.
In all cases, material and supplies will be trucked to the various facilities using primarily diesel fuel. Orders for Sterile Talc Powder will be shipped by truck or airfreight.

There is no habitat of an endangered or threatened species close enough to the U.S. distribution point for there to be a significant effect. Transport, use, and disposal (recycling) of the material and the bottles will take place across the entire United States, but amounts in anyone location will be small enough so as to have no significant effect on any endangered or threatened species in that location.

The Center for Drug Evaluation and Research has concluded that the product can be used and disposed of without any expected adverse environmental effects. Adverse effects are not anticipated upon endangered species or upon property listed in or eligible for listing in the National Register of Historic Places.

Date: 09-DEC-2003

Prepared by: Josephine M. Jee,
Review Chemist
HFD-150
ONDC/DNDC I

Identification of chemical substances that are the subject of the proposed action:

DRUG SUBSTANCE

Talc

Established or generic name:	Talc
Brand name of talc used:	— Ultra 2000 (As of September 9, 2002 — has been renamed — The name — will be dropped. There will be no change in the produc
Composition:	Talc
CAS Reg. No:	Talc, 14807 -96-6
Molecular formula:	Talc: Mg3 Sil0(OH)2
Description:	Talc USP is a solid, white to gray-white impalpable powder which contains asbestos-free talc and chlorite at a concentration of greater or equal to 95%.
Odor:	None
pH:	Suspension of — in water: pH = —
Solubility: In water	—
Melting Point:	—

The Material Safety Data Sheet (MSDS) for — Ultra 2000 is included in Appendix A.

B.

A Certificate of Analysis for Ultra 2000, Talc USP is provided in Appendix

DRUG PRODUCT

Sterile Talc Powder

Each vial contains a single dose of sterile, asbestos-free talc for instillation, consisting of — of Talc USP.

Talc CAS NO:	14807-96-6
Identification:	conforms to the USP test
Loss on ignition:	it loses not more than — % of its weight.
Acid-soluble substances:	the weight of the residue does not exceed — mg (—

Reaction and soluble substances:	**the weight of the residue does not exceed. —mg (—%).**
Water-soluble iron:	**the liquid does not acquire a blue color.**
Arsenic:	**the limit is — ppm**
Heavy metals:	**the limit is — %.**
Lead:	**not more than — of lead (— %).**
Particle Size Range:	**— % within — µm** **— % within — µm** **— % within — µm**
Physical State:	**Solid, impalpable powder**
Color:	**White to gray-white**
Odor:	**None**
pH:	**Suspension of — % in water: pH = —**
Real Density:	—
Solubility: In water	— %
Melting Point:	— °C

6. Introduction of substances into the environment.

ENVIRONMENT AL CONCERNS CAUSED BY PRODUCTION OF THE BULK DRUG SUBSTANCE

The — Ultra 2000 Talc is mined in — It is extracted manually from the talc deposit at that location then subjected to mechanical powdering operations. The final product has no chemical additives. It is completely characterized as to mineralogical composition and granulometric characteristics in the laboratories of —

—

The entire operation is carried out in accordance with Good Manufacturing Practices (GMP) and is in conformance to — regulations regarding mining. Talc is sold worldwide in large quantities for purposes ranging from use as cosmetics, and' for industrial and pharmaceutical uses. The additional amount needed for the bottles covered by this NDA will not have any adverse effect upon compliance with the current regulations.

ENVIRONMENTAL CONCERNS CAUSED BY FORMULATION AND P ACKAGING OF DRUG PRODUCT:

Bottles are filled with the — of talc at —

— The processes at the plant conform to Good Manufacturing Practices and the Quality System Regulations. All steps are rigorously controlled according to the quality control procedures in place. No adverse environmental effects will result from the filling operation. The bottles required if this NDA is approved will not result in lack of compliance with existing regulations.

Sterilization of the bottles is carried out by — at their facilities in either — They operate according to the exacting standards of Good Irradiation Practice and are routinely inspected and audited by major healthcare manufacturers and regulatory authorities, including the FDA. Their sophisticated in-house control systems guarantee safe and environmentally sound operation at their plants. They are in compliance with all existing regulations applicable to their procedures. Sterilization of additional bottles resulting from the approval of this NDA will not jeopardize that compliance.

ENVIRONMENTAL CONCERNS CAUSED BY USE AND DISPOSAL

Each single dose vial is designed to deliver a — dose of talc to the patient. This talc coats the pleural surfaces and acts to eliminate the pleural effusion. For the most part the talc will remain in place during the remainder of the patient's life (patients with MPE secondary to cancer usually have life expectancies measured in months at most). The talc will not be systemicallyabsorbed and, therefore, will not be excreted.

The amounts involved in this particular use of Talc will be small, since the patient population is small (orphan drug status for the use of talc in MPE has been granted to Bryan Corporation). Bryan Corporation estimates that, after this NDA is approved, in the first year following approval, approximately — bottles are expected to be sold in the first year following approval an it is expected that this will increase by about — per year thereafter.

7. Fate of emitted substances in the environment:

Talc

The talc in the vial is a solid, in powder form, which is inert and relatively insoluble. For use the talc must be made into a slurry by the addition of sterile - saline. The slurry is drawn up into two syringes then instilled in the pleural cavity through a chest tube. After instillation into the pleural cavity, it will remain on the pleural surfaces where it acts as a sclerosing agent and reduces the effusions. It is not systemically absorbed; therefore it will not be excreted. The bulk of the substance will remain in the patients lungs for the length of time that the MPE patient lives.

(a) Air

Unless the vial is broken, very little, if any of the talc will enter the air. Amounts that do become airborne due to breakage of the vial could be spread around due to the powdery nature of the material, but they will ultimately fall to the ground or local surfaces in the area in which the break occurred.

(b) Water

Talc is very sparingly soluble in water. No significant amount will enter the aquatic compartment.

(c) Terrestrial ecosystems

Talc is a naturally occurring chemically inert substance. Any amounts that do become airborne and later settle to the ground wi" not react with any other substance that they come in contact with.

8. Environmental effects of released substances

a) Air

The talc used will not have any adverse effect on the atmosphere.

(b) Water

The talc used will not have any adverse effect on the aquatic environment. The likelihood of this material reaching the aquatic environment is very small.

(c) Terrestrial ecosystems

The talc used will not have any adverse effect on terrestrial ecosystems.

9. Use of resources and energy

Water and electricity are used in the mining operations. Trucks at the site are probably diesel-powered. The incremental amounts of resources and energy used at the quarry to supply the talc for Bryan Corporation are not a significant amount of the overall usage.

— where the bottles are filled and packaged uses electricity and water.

— where the product is sterilized will use electricity and a source of gamma irradiation.

Use of the bottles will not require natural resources or energy.
Disposal of used bottles into the recycling stream will entail use of electricity as well as diesel fuel for the trucks used to haul this type of waste.

In all cases, material and supplies will be trucked to the various facilities using primarily diesel fuel. Orders for Sterile Talc Powder will be shipped by truck or airfreight.

There is no habitat of an endangered or threatened species close enough to the U.S. distribution point for there to be a significant effect. Transport, use, and disposal (recycling) of the material and the bottles will take place across the entire United States, but amounts in anyone location will be small enough so as to have no significant effect on any endangered or threatened species in that location

The distribution site in Massachusetts is not close to any properties listed in or eligible for listing in the National Register of Historic Places. Therefore, distribution activities will not adversely effect any historic sites. Transport, use and disposal of the material will be nationwide, but the amounts at any one location will not affect any historic places, assuming that existing highways, storage facilities and recycling stations have all been sited with reference to the impact on historic places in the area.

10. Mitigation measures

The mining of the talc and the manufacture and sterilization of the Sterile Talc Powder bottles are all performed under strict controls, reducing the introduction of any waste materials into the environment.
U se of this product causes no environmental damage. The talc is inert and remains in the patients lungs.

This product is not a major hazard to the environment, in its manufacture, distribution, use, or disposal, particularly given the amounts projected for the use described in this NDA. No mitigation measures at any stage of the process described would reduce environmental damage caused by the product as presently constituted.

11. Alternatives to the proposed action:

An alternative which would prevent any possible contamination of the environment by this drug product would be to discontinue manufacturing and not introduce the product into the market. However, this course of action would remove a useful dosage form of a proven treatment for the serious condition, malignant pleural effusions.

12. List of preparers:

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Waldman Biomedical Consultancy, Inc.
Oceanside, New York

Jane B. Campbell
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13. Certification:

The undersigned official certifies that the information presented is true, accurate, and complete to the best of the knowledge of the firm or agency responsible for preparation of the environmental assessment.

Date September 17, 2002 Signature of Responsible Official

14. References
None

15. Appendices

Appendix A: Material Safety Data Sheet for Ultra 2000, Talc USP Appendix B: Certificate of Analysis for Ultra 2000, Talc USP

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Josephine Jee
12/9/03 06:35:07 PM
CHEMIST

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