CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-388

Administrative/Correspondence

SECTION 14

PATENT CERTIFICATION

INDEX

14. PATENT CERTIFICATION

In the opinion of, and to the best knowledge of, Bryan Corporation, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

SECTION 16

DEBARMENT CERTIFICATION

INDEX

16.1 CERTIFICATION STATEMENT

In accordance with Section 306(k)(1) of the Food, Drug and Cosmetic Act, 21 U.S.C. Section 335a(k)(1), Bryan Corporation certifies that it did not and will not use in any capacity the services of any person debarred under sections 306(a) or 306(b), in connection with this application.

EXCLUSIVITY SUMMARY for NDA # 21-388 SUPPL #

Trade Name Sterile Talc Powder®

Generic Name sterile talc powder

Applicant Name Bryan Corporation HFD- 150

Approval Date

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_X__/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /_X_/

      If yes, what type(SE1, SE2, etc.)?

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /_X_/ NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /___/ NO /_X_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /__/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /_X_/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-587 Sclerosol Intrapleural Aerosol®

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /_X_/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as

bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /_**X**_/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study #

Investigation #2, Study #

Investigation #3, Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /__/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /__/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #

NDA # _____ Study #

NDA # _____ Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study #

Investigation #__, Study #

Investigation #__, Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # ___ YES /___/ ! NO /___/ Explain:

Investigation #2

IND # _____ YES /___/ ! NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

/S/

Sean Bradley, R.Ph.
Regulatory Health Project Manager

JONEC03
Date

/S/

Richard Pazdur, M.D.
Division Director

12/15/03
Date

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA # : 21-388

amp Date: July 07, 2003 Action Date: December 15, 2003

HFD 150 Trade and generic names/dosage form: Sterile Talc Powder

Applicant: Bryan Corporation Therapeutic Class: Sclerosing Agent

Indication(s) previously approved: Prevention of the recurrence of malignant pleural effusions in symptomatic patients

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): one

Indication #1: Sclerosing agent to decrease the recurrence of malignant pleural effusions in symptomatic patients

Is there a full waiver for this indication (check one)?

X Yes: Please proceed to Section A.

☐ No: Please check all that apply: ____Partial Waiver ____Deferred ____Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
X Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
X Other: Orphan Drug

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min____	kg____	mo.____	yr.____	Tanner Stage____
Max____	kg____	mo.____	yr.____	Tanner Stage____

Reason(s) for partial waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
☐ Adult studies ready for approval
☐ Formulation needed
☐ Other:_____

studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is mplete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min ____ kg____ mo.____ yr.____ Tanner Stage_____
Max____ kg____ mo.____ yr.____ Tanner Stage_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min ____ kg____ mo.____ yr.____ Tanner Stage_____
Max____ kg____ mo.____ yr.____ Tanner Stage_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

_____
Regulatory Project Manager

cc: NDA
HFD-960/ Terrie Crescenzi
(revised 1-18-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-388	Efficacy Supplement Type SE-	Supplement Number
Drug: **Sterile Talc Powder®**	Applicant: **Bryan Corporation**	
RPM: **Bradley, Sean**	HFD-150	Phone # **301-594-5770**
Application Type: ( ) 505(b)(1) (X) 505(b)(2)	Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	( ) Standard (X) Priority
• Chem class (NDAs only)	**Sclerosing agent**
• Other (e.g., orphan, OTC)	**Orphan**
❖ User Fee Goal Dates	**March 21, 2003**
❖ Special programs (indicate all that apply)	( ) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	( ) Paid
• User Fee waiver	(X) Small business **11FEB02** ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	(X) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) (X) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified
❖ Exclusivity Summary (approvals only)	**N/A**
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	**N/A**

General Information	
Actions	
• Proposed action	( ) AP ( ) TA (X) AE ( ) NA
• Previous actions (specify type and date for each action taken)	
• Status of advertising (approvals only)	( ) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes (X) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	( ) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	-------
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	-------
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	-------
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	-------
• Applicant proposed	X
• Reviews	X
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	-------
• Documentation of discussions and/or agreements relating to post-marketing commitments	-------
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	-------
• Pre-NDA meeting (indicate date)	29MAR01
• Pre-Approval Safety Conference (indicate date; approvals only)	-------
• Other	-------
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	**Medical TL 20MAR03**
❖ Clinical review(s) *(indicate date for each review)*	**20MAR03**
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	—
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	**page 36 of medical review**
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	**N/A**
❖ Statistical review(s) *(indicate date for each review)*	**Joint statistical/medical review**
❖ Biopharmaceutical review(s) *(indicate date for each review)*	**07MAR03**
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	**N/A**
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	—
• Bioequivalence studies	—
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	**Review #1 - 19MAR03** **Review #2 – 21MAR03**
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	**19MAR03**
• Review & FONSI *(indicate date of review)*	—
• Review & Environmental Impact Statement *(indicate date of each review)*	—
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	**20MAR03**
❖ Facilities inspection (provide EER report)	Date completed: (X) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed ( ) Requested (X) N/A
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	**January 2, 2003/January 3, 2003**
❖ Nonclinical inspection review summary	—
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	—
❖ CAC/ECAC report	—

Office Director's Memo

This application will be signed off at the Division level.

From the American Society of Clinical Oncology.
In collaboration with the Food and Drug Administration (FDA), and as a service to our members, ASCO will provide information about newly approved therapies for cancer patients. This will allow the agency to inform oncologists and professionals in oncology-related fields of recent approvals in a timely manner. Included in the email from the FDA will be a link to the product label, which will provide the relevant clinical information on the indication, contraindications, dosing, and safety. The following is a message from Dr. Richard Pazdur:

To: ASCO membership (domestic USA, embargo date 12/??/03)

From: Richard Pazdur, M.D.
Director, Division of Oncology Drug Products,
Center for Drug Evaluation and Research, FDA

On December 15, 2003 the U.S. Food and Drug Administration approved Sterile Talc Powder (Bryan Corporation), administered intrapleurally via chest tube, as a sclerosing agent to decrease the recurrence of malignant pleural effusions in symptomatic patients.

The data demonstrating safety and efficacy are from the published medical literature. There were five randomized studies that were designed to evaluate the risk of recurrence of malignant pleural effusions in patients with a variety of solid tumors. For each study, talc slurry was compared with a concurrent control, using a prospectively defined objective measure of "success." For the 89 evaluable patients studied in the 5 randomized controlled trials, there was an 89% success rate (range 79-100%). Thirteen additional single arm trials and retrospective series from the literature are also supportive of efficacy with variously defined "success" rates ranging from 75-100%.

Adverse events (AEs) most frequently reported in the literature in association with intrapleurally administered talc slurry are fever and pain. Acute pneumonitis and Acute Respiratory Distress Syndrome (ARDS) have been reported in association with intrapleural talc administration.

Sterile Talc Powder should be administered after adequate drainage of the effusion. The success of pleurodesis appears to be related to the completeness of drainage of the pleural fluid, as well as the full re-expansion of the lung. The recommended dose is 5 g, dissolved in 50-100 ml of sodium chloride solution. Although the optimal dose for effective pleurodesis is unknown, 5 g was the dose most frequently reported in the published literature.

The only other licensed formulation of talc (Sclerosol Intrapleural Aerosol) is packaged with a chlorofluorocarbon (CFC) propellant for direct insufflation into the open pleural surface intraoperatively or during thoracoscopy.

Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at www.fda.gov/cder/foi/label/2003/021388lbl.pdf

The approval announcement itself will also be available at www.fda.gov/cder/cancer/whatsnew.htm

For further information related to oncology drug approvals, regulatory information, and other oncology resources, please refer to the FDA "Oncology Tools" web site at www.fda.gov/cder/cancer.

"ASCO periodically e-mails its membership messages of professional interest. If you would prefer not to receive these messages, reply to this e-mail with the word REMOVE in the subject field. You will receive one additional e-mail message to confirm your removal from this e-mail list."

Redacted 18

pages of trade

secret and/or

confidential

commercial

information

Division of Oncology Drug Products

Team Leader's Review

NDA: 21-388

Sponsor: Bryan Corporation

Drug Product: Sterile Talc Powder

Date submitted: September 20, 2002

Background:

Bryan Corporation submitted this New Drug Application (NDA) for sterile talc powder, This product is a new formulation, a non-aerosolized version of Sclerosol® (NDA 20587), which was approved for the treatment of malignant pleural effusions on December 24, 1997. The only formulation difference between Sclerosol® and sterile talc powder is that Sclerosol® contains dichlorofluoromethane (CFC-12), as a propellant.

The primary efficacy and safety data of this NDA are based on a review of the literature. The sponsor has not performed any new pre-clinical or clinical studies in support of this application.

Chemistry:

Bryan Corporation will supply sterile talc powder in a single use 100-mL glass bottle. Each bottle will contain grams (g) of Talc USP, asbestos-free and bucite-free. The purity of Talc USP will be greater than 95%. Talc USP will be primarily hydrated magnesium silicate. Associated minerals include dolomite, calcite, and quartz. The product is asbestos-free. The particle size of the powder is within . The finished product will be sterilized by gamma irradiation.

Microbiology:

Bryan Corporation failed to validate its sterilization procedure for sterile talc powder. For details, see the Microbiology Review of this NDA.

Preclinical Pharmacology and Toxicology Information:

Multiple published pre-clinical studies have demonstrated that talc slurry produces pleurodesis after intrapleural injection. Review of the published literature did not identify any pre-clinical safety issues; however one article noted the distribution of talc in every organ of the body after intrapleural administration in normal rats. No information exists on impairment of fertility in animals by talc. For details, see the Pharmacology/Toxicology Review of this NDA.

The exact mechanism by which talc produces pleurodesis is not completely understood. Talc may act through the following mechanism. Adsorption onto the pleura results in an inflammatory process which promotes the adherence of the pleural and parietal pleura, obliterating the pleural space and preventing re-accumulation of pleural pleural fluid.

Human Pharmacology:

The sponsor has not performed any pharmacokinetic or pharmacodynamic studies. No published literature exists detailing pharmacokinetic or pharmacodynamic information on talc. Most reported clinical studies have utilized 5 g (range 2 g-10g).

Clinical Summary:

Talc has been used to control pleural effusion for many years. The first published literature describing the use of talc to control pleural effusions dates back to 1935.

The submission contained 5 randomized controlled studies, which compared the effectiveness of talc slurry with chest tube drainage, bleomycin, and talc insufflation for the treatment of malignant pleural effusions arising mostly from breast or lung cancer. The studies compared talc slurry, instilled into the pleural cavity via chest tube, with a concurrent control. In all studies, after maximal drainage of the pleural effusion, the investigator administered talc slurry via the chest tube. Chest films documented response, which was defined as lack of recurrence of the effusion. Studies differed on the timing of the efficacy assessment.

The table below shows the design of the randomized, controlled studies, dose of talc slurry used, and efficacy results. Overall 79/89 (89%) evaluable patients from the randomized, controlled studies had a response to talc slurry pleurodesis.

Randomized Control Studies Using Talc Slurry to Control Malignant Pleural Effusions

REFERENCE	TREATMENT	RESPONSE RATE	RESPONSE RATE

		EVALUABLE PTS[a] p value*	ALL PTS p value*
Sorensen et al. Eur J Respir Dis. 1984; 65(2):131-5	Talc Slurry 10g vs. Chest Tube drainage alone	100% (9/9) vs. 58% (7/12) p = 0.04	64% (9/14) vs. 41% (7/17) p= 0.29
Noppen et al. Acta Clin Belg 1997; 52(4):258-62	Talc Slurry 5g vs. Bleomycin 1mg/kg	79% (11/14) vs. 75% (9/12) p = 1.00	79% (11/14) vs. 75% (9/12) p = 1.00
Zimmer PW et al. Chest 1997; 112(2):430-434	Talc Slurry 5g vs. Bleomycin 60U	90% (17/19 [b]) vs. 79% (11/14 [b]) p = 0.63	Not given
Ong KC et al. Respirology 2000; 5:99-103	Talc Slurry 5g vs. Bleomycin 1 U/kg	89% (16/18) vs. 70% (14/20) p = 0.24	64% (16/25) vs. 56% (14/25) p =0.77
Yim AP et al. Ann Thorac Surg 1996; 62:1655-8	Talc Slurry 5g vs. Talc Insufflation 5g powder	90% (26/29) vs. 96% (27/28) p = 0.61	90% (26/29) vs. 96% (27/28) p = 0.61

*Two-sided p-value based on Fisher's exact test
a Studies differed in definitions of evaluable patients.
b Data per procedure (33 procedures per 29 evaluable patients, 3 patients with bilateral effusions)

Reviewer's Table

The submission also contained fourteen single arm studies, which used talc slurry for the treatment of malignant pleural effusions. The studies differed in their definition of success. The published, single-arm studies reported "success" rates using talc slurry pleurodesis, which ranged from 75-100%.

Review of the literature reports suggest the side effects associated with use of talc slurry include: fever, pain, hypoxemia, dyspnea, unilateral pulmonary edema, acute respiratory distress syndrome, tachycardia, arrhythmia, myocardial infarction, hypotension, hypovolemia, and empyema.

For details, see the Medical Officer's Review of this NDA.

Other Pharmaceutical Products Available

Currently, bleomycin, mechlorethamine (Mustargen), quniacrine hydrochloride (Atabrine) and Sclerosol® are the only approved sclerosing agents. The advantage of sterile talc slurry over bleomycin includes the fact that allergic reactions are not a concern for talc administration. The advantage of sterile talc slurry over Mustargen, a vesicant, is that Mustargen use is associated with extremely painful inflammation whereas talc slurry is not. Quinacrine hydrochloride has not been available or marketed for the last 8-10 years. In January 2003, the holder of the NDA for quinacrine hydrochloride requested that

the NDA be withdrawn. The advantage of sterile talc slurry over Sclerosol® includes the fact that it can be administered at the bedside via a chest tube, whereas Sclerosol® requires thoracoscopy for administration, which usually is performed in an operating room and requires anesthesia. An additional advantage of talc slurry over Sclerosol® is the concern about ozone depletion with the use of CFC containing products. Because of an international treaty banning the use of CFC- containing propellants Sclerosol® will be discontinued shortly.

Conclusions and Recommendations

Review of the literature suggests that the treatment of malignant pleural effusions can bring effective palliation of patient's symptoms. For many years, some formulation of talc has been used to treat pleural effusions in symptomatic patients. The literature review submitted for this NDA suggests that the talc slurry formulation is effective in reducing the risk of recurrent pleural effusions.

Because of the unresolved sterility issues, I concur with the primary medical officer's review and recommend that Bryan Corporation receive an approvable letter for sterile talc powder as a sclerosing agent to reduce the risk of recurrence of malignant pleural effusions in symptomatic patients.

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

/s/

Ann Farrell
3/19/03 08:37:36 AM
MEDICAL OFFICER

Grant Williams
3/20/03 08:03:01 AM
MEDICAL OFFICER

REGULATORY PROJECT MANAGER REVIEW

Application Number: 21-388

Name of Drug: Sterile Talc Powder

Sponsor: Bryan Corporation

Material Reviewed

- Labeling (AF) submitted by Bryan Corporation c/o Waldman Biomedical Consultancy, Inc., September 30, 2003
- Final Printed Labeling (FPL) submitted by Bryan Corporation c/o Waldman Biomedical Consultancy, Inc., October 15, 2003 which supercedes the FPL submitted October 08, 2003

Background and Summary Description:

Sterile Talc Powder, administered intrapleurally via chest tube, is indicated as a sclerosing agent to decrease the recurrence of malignant pleural effusions in symptomatic patients. The original application received an approvable action on March 21, 2003 pending microbiological corrections.

In the approvable letter, the FDA requested final printed labeling be submitted identical to the agreed upon labeling included in the letter. Bryan originally submitted the requested final printed labeling (BL) on July 31, 2003, but it was not approved because non-FDA approved changes were made to the labeling.

Bryan submitted final printed labeling (FPL), dated October 15, 2003 for FDA approval.

Review

The October 15, 2003 labeling is identical to the labeling submitted to the Agency September 30, 2003 and accepted October 15, 2003. Therefore, this FPL should be approved with the NDA.

Sean Bradley, R.Ph./20OCT03
Regulatory Health Project Manager

Concurrence:

Dotti Pease/05NOV03
Chief, Project Management Staff

Ann Farrell, MD/05NOV03
Medical Team Leader

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

/s/

Sean Bradley
11/5/03 10:26:20 AM
CSO

REGULATORY PROJECT MANAGER REVIEW

Application Number: 21-388

Name of Drug: Sterile Talc Powder

Sponsor: Bryan Corporation

Material Reviewed

- Finalized FDA suggested labeling included in the March 21, 2003 NDA Approvable Letter
- Final Printed Labeling (BL) submitted by Bryan Corporation c/o Waldman Biomedical Consultancy, Inc., on July 31, 2003
- Revised Labeling (AF) submitted by Bryan Corporation c/o Waldman Biomedical Consultancy, Inc., on September 30, 2003

Background and Summary Description:

Sterile Talc Powder, administered intrapleurally via chest tube, is indicated as a sclerosing agent to decrease the recurrence of malignant pleural effusions in symptomatic patients. The original application received an approvable action pending microbiological corrections.

In the approvable letter, the FDA requested final printed labeling be submitted and identical to the agreed upon labeling included in the letter. Bryan originally submitted the requested final printed labeling (BL) on July 31, 2003, but it was not approved because non-FDA approved changes were made to the labeling.

Byran resubmitted revised labeling (AF), dated September 30, 2003 in response to the Agency's September 26, 2003 request for revised labeling.

Review

July 31, 2003 (BL)

The FPL submitted by Bryan was compared with the final approved labeling included in the Agency's NDA approval letter. There following differences are outlined below for medical reviewer review. Differences are underlined.

1. The labeling has been updated to reflect the amount of Sterile Talc Powder contained in each package bottle from ~g to 5 g.

    - **Approved by medical team leader 20AUG03**

2. In the **DESCRIPTIONS** section:

   FDA version-
   [redacted]

   Bryan version-
   Sterile Talc Powder is a sclerosing agent intended for intrapleural administration supplied in a single use, 100 mL brown glass bottle

   - **Approved by medical team leader 20AUG03**

3. In the **PRECAUTIONS** section:

   FDA version-
   3. **Pulmonary complications:** Acute Pneumonitis and Acute Respiratory Distress Syndrome (ARDS) have been reported in association with intrapleural talc administration.

   Bryan version-
   3. [redacted]

   - **NOT Approved by medical team leader 20AUG03**

4. In the **DOSAGE AND ADMINISTRATION** section, **Talc Preparation** subsection:

   A. Aseptic technique **has not been bolded** as in the FDA suggested version:

      Bryan's version-
      Prepare the talc slurry using aseptic technique in an appropriate laminar flow hood. Remove talc container from packaging. Remove protective flip-off seal.

      - **Approved by medical team leader 20AUG03**

   B. #4 of Talc preparation instructions:

      FDA version-
      statement "For Pleurodesis Only - NOT FOR IV ADMINISTRATION ",

      Bryan version-
      statement [redacted]

- **NOT Approved by medical team leader 20AUG03**

5. In the **DOSAGE AND ADMINISTRATION** section, **Administration** subsection:

   The parenthesis have been removed from the following statement in the Bryan version:

   FDA version-
   Following introduction of the talc slurry, the chest drainage tube is clamped, and the patient is asked to move, at 20 to 30 minute intervals, from supine to alternating decubitus positions, so that over a period of about 2 hours the talc is distributed within the chest cavity. (Recent evidence suggests that this step may not be necessary.)

   Bryan version-
   Following introduction of the talc slurry, the chest drainage tube is clamped, and the patient is asked to move, at 20 to 30 minute intervals, from supine to alternating decubitus positions, so that over a period of about 2 hours the talc is distributed within the chest cavity. Recent evidence suggests that this step may not be necessary.

- **Approved by medical team leader 20AUG03**

Conclusion

Due to unapproved changes in the sponsor submitted FPL, this proposed label should not be approved.

Sean Bradley, R.Ph./20AUG03
Regulatory Health Project Manager

September 30, 2003 (AF)

This labeling includes the following Agency suggested labeling changes:

1. In the **PRECAUTIONS** section:

   From-
   Bryan version-

   To-
   FDA version-
   Pulmonary complications: Acute Pneumonitis and Acute Respiratory Distress Syndrome (ARDS) have been reported in association with intrapleural talc administration.

2. In the **DOSAGE AND ADMINISTRATION** section, **Talc Preparation** subsection:

   #4 of Talc preparation instructions:

   From-
   Bryan version-
   [redacted]

   To-
   FDA version-
   statement "For Pleurodesis Only - NOT FOR IV ADMINISTRATION ",

Conclusion

Based on the corrections made in this (AF) submission, I suggest that this package labeling for Sterile Talc Powder™ be approved.

Sean Bradley, R.Ph./09OCT03
Regulatory Health Project Manager

Concurrence:

Dotti Pease/09OCT03
Chief, Project Management Staff

Ann Farrell, MD/10OCT03
Medical Team Leader

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

/s/

Sean Bradley
10/15/03 11:21:52 AM
CSO

Ann Farrell
10/15/03 01:36:29 PM
MEDICAL OFFICER

12 pages redacted from this section of the approval package consisted of draft labeling

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: December 30, 2002	**DUE DATE:** February 15, 2003	**ODS CONSULT #:** 02-0256

TO: Richard Pazdur, M.D.
Director, Division of Oncology Drug Products
HFD-150

THROUGH: Sean Bradley
Project Manager
HFD-150

PRODUCT NAME: **Sterile Talc Powder—grams** **NDA: 21-388**	**NDA SPONSOR:** Bryan Pharmaceuticals

SAFETY EVALUATOR: Denise P. Toyer, Pharm.D.

SUMMARY: In response to a consult from the Division of Oncology Drug Products (HFD-150), the Division of Medication Errors and Technical Support (DMETS) conducted a labeling review of the container labels, carton and insert labeling for the drug product "Sterile Talc Powder" for possible interventions to minimize medication errors with the use of the product.

DMETS RECOMMENDATION:

DMETS recommends revising the labels and labeling as outlined in Section II of this review.

/S/

Carol Holquist, RPh
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

CONTAINER LABEL AND CARTON/INSERT LABELING REVIEW

DATE OF REVIEW: February 10, 2003

NDA # 21-388

NAME OF DRUG: Sterile Talc Powder — grams

NDA HOLDER: Bryan Pharmaceuticals

I. INTRODUCTION:

This consult was written in response to a request from the Division of Oncology Drug Products, to review the container labels, carton and insert labeling for Sterile Talc Powder. The draft vial labels, pouch, carton, and package insert labeling were reviewed for possible interventions to minimize medication errors.

PRODUCT INFORMATION

Sterile Talc Powder is a sclerosing agent that is administered intrapleurally. It is indicated to [redacted] Sterile Talc Powder is instilled into the pleural cavity and induces an inflammation reaction. The inflammation reaction promotes adherence of the visceral and parietal pleura. The pleural space is obliterated and prevents re-accumulation of pleural fluid. The recommended dose of Sterile Talc Powder ranges from — grams (in one-gram increments) diluted in normal saline. The product is supplied in - gram vials of Sterile Talc Powder. When each vial is reconstituted with — milliliters of sodium chloride for injection the final concentration is 100 mg per mL of Sterile Talc Powder as a slurry.

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, pouch, carton, and insert labeling of "Sterile Talc Powder," DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. The strength of the product (i.e., — grams) should be relocated so that it appears immediately following the established name. For example:

Sterile Talc Powder
— gm/vial

2. Revise the "Caution: Federal law prohibits dispensing..." to read "Rx Only."

B. VIAL LABEL

1. See General Comments above.

2. The wording [ ] should be revised to read 'For Intrapleural Administration Only.' This information should be provided in a bold font.

3. If space permits include the storage recommendations.

4. DMETS recommends that the statement [ ] be removed from the label. This information may confuse practitioners [ ] — nL is actually needed).

5. DMETS recommends that the statements [' and]' be removed. These statements clutter the label and removal would provide necessary space for important information such as instructions for reconstitution.

6. Include the directions for reconstitution and the resulting concentration [ ]

C. POUCH LABELING

1. See Comments B-1 through B-6.

2. [

]

D. CARTON LABELING

1. See Comments B-1 through B-6.

2. See Comment C-2.

3. The packaging carton is — The carton labeling — will only be displayed on one of

[ ] DMETS recommends that the carton labeling also be displayed on other panels of the packaging carton (e.g., front, top, and other end).

E. PACKAGE INSERT LABELING

1. GENERAL COMMENT

When referring to the product strength; it should be expressed without a trailing zero (e.g.,~ gm rather than ~ gm). Revise throughout the insert.

2. DESCRIPTION Section

The second sentence states: 'Each bottle contains a minimum of ~ g of Talc USP.....' This statement implies that the vial may contain more than what is labeled. Revise accordingly.

3. WARNINGS Section

This section of the labeling should contain a statement informing practitioners that Sterile Talc Powder should not be administered intravenously.

2. DOSAGE AND ADMINISTRATION Section, Direction #4

a. The following sentences should be listed before Direction #3. [ ] For example,

[ ]

[ ]

b. [ ]

[ ]

c. [ ]

[ ]

d. We note, the sponsor indicates that the syringes should be labeled with the following statement 'For Pleurodesis Only – not for IV administration." However, it is possible that pharmacies will use the same label for Sterile Talc Powder *Irrigation* syringes as they use for other intravenous preparations that are dispensed in syringes. DMETS notes that the irrigation syringe has a difference appearance, however the potential for medication errors due to confusion between the irrigation and intravenous syringes and routes of administration exists. We recommend that the sponsor provide auxiliary labels, perhaps brightly colored stickers with the aforementioned information pre-printed on them to prevent the potential for administration of the irrigation solution intravenously.

III. RECOMMENDATIONS:

DMETS recommends revising the labels and labeling as outlined in Section II of this review.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

/S/

Denise P. Toyer, Pharm.D.
Safety Evaluator/Team Leader
Division of Medication Errors and Technical Support

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

/s/

Denise Toyer
2/10/03 09:05:46 AM
PHARMACIST

Carol Holquist
2/10/03 10:31:13 AM
PHARMACIST

Jerry Phillips
2/10/03 03:30:34 PM
DIRECTOR

SECTION 18

USER FEE COVER SHEET

INDEX

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

Form Approved OMB No. 0910-0297
Expiration Date: February 29, 2004

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Bryan Corporation
Four Plympton Street
Woburn, MA 01801

2. TELEPHONE NUMBER *(Include Area Code)*

(800) 343-7711

3. PRODUCT NAME

Sterile Talc Powder

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

N021388

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☐ YES ☒ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA)

6. USER FEE I.D. NUMBER

Not Required

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE **EXCLUSIONS**? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory)

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☒ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☒ YES ☐ NO

(See item 8, reverse side if answered YES)

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Alan A. Waldman	President, Waldman Biomedical Consultancy, Agent for Bryan Corp.	August 15, 2002

Advisory Committee Meeting Minutes

This application was not the subject of an Advisory Committee Meeting.

N-000-BC ORIGINAL

Waldman Biomedical Consultancy, Inc.

Serving the Health Care Industry World-Wide℠

October 20, 2003

Document Mail Center
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncological Drug Products
(HFD-150)
1451 Rockville Pike
Rockville, MD 20852

Attn: Mr. Sean Bradley

RE: **Response to Information Request for Sterile Talc Powder - NDA 21-388**

Dear Mr. Bradley,

In a FAX dated October 17, 2003 the Agency inquired as to the status of Bryan Corporation's Sclerosol Intrapleural Aerosol following approval of Sterile Talc Powder as follows:

> "Regarding your currently marketed drug product Sclerosol Intrapleural Aerosol: if your new talc product is approved, what will happen to the Sclerosol? Will you continue to make it? What is your current inventory and the estimated months supply of Sclerosol?"

Bryan Corporation intends to continue making and marketing Sclerosol Intrapleural Aerosol following the approval of Sterile Talc Powder.

At this time there are — in current inventory. Based on current demand, this is approximately — supply. —
— inventory up to approximately —
usage this will last approximately — It is expected, however, —

If there are any questions regarding this labeling or if additional copies are desired, please don't hesitate to contact us at (516) 763-1158 or at the contact points in the letterhead.

Best regards,

Yours truly,

Alan A. Waldman

Alan A. Waldman, Ph.D.
President
Waldman Biomedical Consultancy, Inc.
Agent for Bryan Corporation

• 516-763-1158 • FAX 516-536-7628

Fax

DIVISION OF ONCOLOGY DRUG PRODUCTS

Center for Drug Evaluation and Research, HFD-150
Woodmont Office Complex - Two
1451 Rockville Pike, Rockville, MD 20852

To: Jane Campbell/Alan Waldman	**From:** Sean Bradley, CSO
Fax: 845-469-4212/516-536-7628	**Fax:** 310-827-4590
Phone: 845-469-4289	**Phone:** 301-594-5770
Pages, including cover sheet: 1	**Date:** October 17, 2003
Re: NDA 21-388-Information Request	

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

Please refer to your July 3, 2003 NDA resubmission for Sterile Talc Powder, number 21-388.

Regarding your currently marked drug product Scerosol Intraplerual Aerosol; if your new talc product is approved, what will happen to the Sclerosol? Will you continue to make it? What is your current inventory and the estimated months supply of Sclerosol?

If you have any questions, please contact me at 301-594-5770 or BradleyS@CDER.FDA.GOV.

Sean Bradley, R.Ph.

Regulatory Project Manager

N-000-AF

ORIGINAL

Waldman Biomedical Consultancy, Inc.℠

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October 15, 2003

Document Mail Center
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncological Drug Products
(HFD-150)
1451 Rockville Pike
Rockville, MD 20852

RECEIVED
OCT 16 2003
DDR-150/CDER

Attn: Mr. Sean Bradley

RE: **FPL - Final printed and electronic copies of the Package Insert for Sterile Talc Powder - NDA 21-388 With changes requested by FDA 10/9/03.**

Dear Mr. Bradley,

As requested in a telephone conversation with the Agency on October 9, 2003, Bryan Corporation has revised the Package Insert for Sterile Talc Powder to correct a typographical error in the Adverse Events section. We are hereby providing hard copies of the final printed labeling for inclusion in the NDA file 21-388 for Bryan Corporation's Sterile Talc Powder.

As directed in the FDA's Action Letter for Sterile Talc Powder NDA 21-388 that was received in a FAX dated 3/24/03, Bryan Corporation is providing 20 paper copies of the Final Printed Package Insert: 10 of the 20 copies have been individually mounted on heavy-weight paper and the additional 10 copies are provided in a closed file envelope.

We are also providing at this time an electronic version of the insert. This is in response to the Agency's call today October 15, 2003.

In addition, also as directed in the FDA's Action Letter, we will be providing under separate cover to the Division of Drug Marketing, Advertising and Communications, two copies of the package insert.

If there are any questions regarding this labeling or if additional copies are desired, please don't hesitate to contact us at (516) 763-1158 or at the contact points in the letterhead.

Best regards,

Yours truly,

Alan A. Waldman

Alan A. Waldman, Ph.D.
President
Waldman Biomedical Consultancy, Inc.
Agent for Bryan Corporation

P.O. Box 575 • Oceanside, New York 11572 • 516-763-1158 • FAX 516-536-7628

Waldman Biomedical Consultancy, Inc.
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October 8, 2003

ORIGINAL
N-000-AF

RECEIVED
OCT 9 2003
DDR-150/CDER

Document Mail Center
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncological Drug Products
(HFD-150)
1451 Rockville Pike
Rockville, MD 20852

Attn: Mr. Sean Bradley

RE: **FPL - Final Printed Package Insert for Sterile Talc Powder - NDA 21-388**
With changes requested by FDA 9/25/03

Dear Mr. Bradley,

As promised in our letter dated September 30, 2003 we are hereby providing hard copies of the final printed labeling for Bryan Corporation's Sterile Talc Powder. As directed in the FDA's Action Letter for Sterile Talc Powder NDA 21-388 that was received in a FAX dated 3/24/03, Bryan Corporation is providing 20 paper copies of the Final Printed Package Insert: 10 of the 20 copies have been individually mounted on heavy-weight paper and the additional 10 copies are provided in a closed file envelope.

We are also providing at this time updated copies of the vial, pouch and carton labeling that reflects the change from – g to 5 g fill. This is in response to the Agency's FAX dated October 6, 2003.

In addition, also as directed in the FDA's Action Letter, we will be providing under separate cover to the Division of Drug Marketing, Advertising and Communications, two copies of the package insert.

If there are any questions regarding this labeling or if additional copies are desired, please don't hesitate to contact us at (516) 763-1158 or at the contact points in the letterhead.

Best regards,

Yours truly,

Alan A. Waldman, Ph.D.
President
Waldman Biomedical Consultancy, Inc.
Agent for Bryan Corporation

Fax

DIVISION OF ONCOLOGY DRUG PRODUCTS

Center for Drug Evaluation and Research, HFD-150
Woodmont Office Complex - Two
1451 Rockville Pike, Rockville, MD 20852

To: Jane Campbell/Alan Waldman	**From:** Sean Bradley, CSO
Fax: 845-469-4212/516-536-7628	**Fax:** 310-827-4590
Phone: 845-469-4289	**Phone:** 301-594-5770
Pages, including cover sheet: 1	**Date:** October 6, 2003
Re: NDA 21-388-Information Request	

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

Please refer to your July 3, 2003 NDA resubmission for Sterile Talc Powder, number 21-388.

Please submit updated copies of the vial, pouch, and carton labeling to reflect the ~~3~~ 5g change.

If you have any questions, please contact me at 301-594-5770 or BradleyS@CDER.FDA.GOV.

Sean Bradley, R.P.h.
/S/
Regulatory Project Manager

N-000-AF

ORIGINAL

Waldman Biomedical Consultancy, Inc.

Serving the Health Care Industry World-Wide℠

September 30, 2003

Document Mail Center
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncological Drug Products
(HFD-150)
1451 Rockville Pike
Rockville, MD 20852

RECEIVED
OCT 2 2003
DDR-150/CDER

Attn: Mr. Sean Bradley

RE: Response to Labeling Revision Request
Final Printed Package Insert for Sterile Talc Powder - NDA 21-388

Dear Mr. Bradley,

Bryan Corporation agrees to the changes to the package insert for Sterile Talc Powder required by the FDA in its FAX dated September 26, 2003

Bryan Corporation has revised the Package Insert for Sterile Talc Powder to reflect the two changes noted in the Agency's Labeling FAX. Attached is a copy of the revised wording that will appear in the final printed labeling (FPL) that is currently being printed.

As soon as the final printed labeling is available, Bryan Corporation will provide 20 paper copies of the FPL. As directed in the Action Letter for of NDA 21-388 that was received in a FAX dated 3/24/03, 10 of the 20 copies will be individually mounted on heavy-weight paper; the additional 10 copies will be provided in a closed file envelope.

Also as directed in the FDA's Action Letter, we will be providing under separate cover to the Division of Drug Marketing, Advertising and Communications, two copies of the package insert.

If there are any questions regarding this labeling or if additional copies are desired, please don't hesitate to contact us at (516) 763-1158 or at the contact points in the letterhead.

Best regards,

Yours truly,

Alan A. Waldman, Ph.D.
President
Waldman Biomedical Consultancy, Inc.
Agent for Bryan Corporation

N-000-BC ORIGINAL

Waldman Biomedical Consultancy, Inc.

Serving the Health Care Industry World-Wide℠

September 30, 2003

Dr. Richard Pazdur, MD
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncological Drug Products (HFD-150)
Office of the Director
1451 Rockville Pike
Rockville, MD 20852

RECEIVED
OCT 2 2003
DDR-150/CDER

Attn: Mr. Sean Bradley

Re New Drug Application - 21-388 for Sterile Talc Powder
Responding to FDA Information Request dated September 25, 2003

Dear Mr. Bradley,

We are hereby responding to the issues noted in FDA's Information Request for NDA 21-388 that was received by Bryan Corporation in a FAX dated 9/25/03.

Three copies of this response will also be provided in hard copy, each containing a copy of the original FAX from the FDA.

In a separate FAX dated 9/26/03 the Agency requested changes to the Final Printed Labeling. Bryan Corporation has agreed to make these changes and, in a separate response to the Agency we are providing a copy of the revised final printed labeling. As soon as final printed copies become available they will be provided to the Agency as requested.

If there are any questions regarding the information provided, or if the Agency would like any additional copies of this amendment, please don't hesitate to call on us at (516) 763-1158 or at the contact points in the letterhead. We look forward to receiving final approval for Sterile Talc Powder.

Best regards,

Yours truly,

Alan A. Waldman

Alan A. Waldman, Ph.D.
President
Waldman Biomedical
Consultancy, Inc.
Agent for Bryan Corporation

P.O. Box 575 • Oceanside, New York 11572 • 516-763-1158 • FAX 516-536-7628