

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-587

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14. PATENT CERTIFICATION: NOT APPLICABLE

REQUEST FOR TRADEMARK REVIEW

RHW
11-22-95

536

TO: Labeling and Nomenclature Committee
Attention: ~~Ms. Yana Mille~~, Chair, ~~HFD-600, MPN-PI~~
MR. DANIEL BORING HFD-530

FROM: Division of Oncologic Drug Product HFD-150
Attention: Bob Barron Phone: 827-1548

DATE: November 21, 1995

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

Proposed Trademark: ~~Bio Talc~~ ^{le} sclerosol ~~BIO TALC~~ NDA/ANDA#: 20-587
RB

Established name, including dosage form: Sterile Aerosol Talc

Other trademarks by the same firm for companion products: None

Indications for use (may be a summary if proposed statement is lengthy):

product will be used as sclerosing agent indicated for malignant pleural effusion secondary to malignancies having spread to the pleural space. Patient prognosis is generally not good.

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

Product is available in Europe as Mucosol, but regulatory status unknown in that market (as IND, devise, etc.).

Name suggested by reviewer in this Division: Aero-Talc. ^{TW}

Attach is instructions for use of this product.

cc: NDA 20-587
HFD-150/Div. File
HFD-150/RPBarron
HFD-150/DCatterson

MEMO OF TELECON

DATE: February 8, 1995

BETWEEN: Ann Sayigh, Parexel
and Alison Martin, M.D., HFD-150
Robert Meyer, M.D., HFD-150
Dotti Pease, HFD-150 *DWP*

SUBJECT: Sterile Aerosolized Talc - Proposed Paper NDA

This telecon was arranged in follow-up to the 2-3-95 telecon to clarify issues regarding the following:

1. **Clinical literature sources with asbestos-free talc vs. references on talc with asbestos.** In the mid 1970's, talc suppliers began removing talc from their product. Sponsor was concerned that many of the literature references dating before the 1970s would be on talc with asbestos and felt that these were therefore not pertinent to this literature review. In addition, these older articles were not written according to today's standards for presenting data. Finally, literature from before 1967 is not computerized and will be difficult to find and review.

We responded that she should make a judgment re: which literature sources to present and make a case in the NDA for why the choices were made. In general, it would depend on the number and quality of references being deleted from the review.

2. Similarly, the **pre-clinical literature** appears to be largely irrelevant, i.e. studied as a food source ingredient, not as a drug. *J. De George* has looked at talc in great detail, but their report does not supply source documents.

Our response was the same as above - Parexel should put together the best case they can for the NDA and give reasons for what was done.

3. Regarding **other possible data**, Parexel has contacted Dr. Colt, who published an article on aerosolized talc in December 1994, but he has no raw data. 11/12 patients improved on talc. Parexel will also try to contact the investigator of the Indiana study and the Lahey Clinic to see if they have any data available. There are 3 abstracts from European studies, but they are not expected to contribute much data, even if the full reports are translated.

cc: AMartin *AM*
RMeyer *J. De George*
WSchmidt
DWPease/2-12-95

CHEMISTRY TEAM LEADER COMMENTS:

NDA 20-587 SCLEROSOL INTRAPLEURAL AEROSOL (STERILE
TALC POWDER)

DIVISION OF ONCOLOGY DRUG PRODUCTS (HFD-150)

OCTOBER 27, 1997

R. H. WOOD, PH.D.

The following comments should be placed in the CMC section of the
approvable NDA letter to be issued today.

Please provide the following information concerning the talc drug product
to the new drug application:

- (1) During an FDA inspection on August 13-19, 1997 of the Sciarra Laboratories, Inc. facility, significant differences were found between the manufacturing procedures described in the NDA for the drug product and those actually being used in the facility. Please provide a current, complete, and detailed manufacturing production record which gives the step-by-step manufacturing instructions, the drug product components to be used, equipment to be used, in-process tests that are performed, and acceptance tests and analytical methods used for all starting components and for the drug product.
- (2) Provide representative, current batch records for drug product manufactured according to the Master Production Record given in (1) above, including the batch numbers, the source and test results for all components used, and analytical results for the drug product tested according to the Sciarra Laboratories, Inc. specifications and methods described in (3) below.
- (3) Provide the regulatory specifications and analytical methods for the drug product manufactured by Sciarra Laboratories (prior to sterilization), including those for satisfactory operation of the valve and actuator, the particle size distribution of the talc aerosol (minimum and maximum size limits as well as size distribution between the

minimum and maximum values), the number of sprays obtained per canister, the amount of talc delivered with each spray, and the microbiological burden for one spray and for the entire canister.

- (4) Provide to the NDA, the acceptance specifications and tests methods used by _____ for the talc drug product prior to sterilization. Provide a detailed, step-by-step copy of the master production record used by _____ for the sterilization of the drug product.
- (5) Provide information on the acceptance tests and methods used by _____ for the talc drug product received from _____ after sterilization. Provide a copy of the step-by-step procedure used by _____ for sterility testing of the drug product, including full information on the sampling plan and testing procedures which are used.
- (6) Provide to the NDA, the current regulatory specifications and analytical methods used by Sciarra for the talc drug product sterilized by _____ and sterility tested by _____. The specifications should include those for the integrity and operation of the valve and accuator components, the integrity of the canister and absence of leakage, the fill and purity of the canister contents, and the consistency and suitability of the talc spray, including particle size distribution range (upper and lower ranges and intermediate distribution values).
- (7) A stability protocol and at least six months of stability data need to be provided for the finished _____ sterilized talc drug product. The data should cover the full range of rads used in the _____ sterilization process and, at appropriate intervals, the device should be taken apart and examined for radiation damage, e.g., to the gaskets and other components and to the inner lining of the canister. The drug product should be examined for possible contamination by the canister lining or device degradation products. The particle size distribution of the talc aerosol should also be monitored as well as other stability-indicating parameters.
- (8) Provide the sampling plans for the selection of representative samples of

the sterilized finished drug product for release testing.

(9) Concerning the bulk talc drug substance obtained from please provide to the NDA the current specifications and analytical methods used by for the talc which is provided to Sciarra Laboratories. Information is also requested on whether the talc must also meet other standards, e.g. those for cosmetics. Provide the current acceptance specifications and test methods used by Sciarra Laboratories for the bulk talc provided by

The above section will replace the Chemist's draft letter comments on the drug product. The Chemist's comments on the drug substance should be added (following the above comments).

/S/

Rebecca H. Wood, Ph.D., Chemistry Team Leader

Distribution:

NDA 20-587 orig

HFD-150 file/ D.Catterson

R.Barron

R.Wood

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 certified 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.

DRUG USAGE IN PEDIATRIC PATIENTS

NDA # 20-587 Trade (generic) names SCLEROSOL™ (STERILE AEROSOL TALC)

Check any of the following that apply and explain, as necessary, on a separate sheet:

- 1. Pediatric studies do not need to be encouraged because the drug product has little potential for use in children (e.g., drugs for angina or Alzheimer's disease).
- 2. Pediatric studies should be done after approval. The drug product has some potential for use in children, but there is no reason to expect early widespread pediatric use (i.e., there are several similar alternative drugs, for example, contrast agents).
 - a. The applicant has committed to doing such studies as will be required to include a pediatric claim in the labeling.
 - (1) We have approved the protocol(s).
 - (2) The protocol(s) has/have been submitted and is/are under review.
 - (3) Protocol design is under discussion with the applicant.
 - (4) The applicant has not yet submitted a protocol.
 - b. The applicant has not committed to doing such studies.
- 4. Pediatric studies designed to provide the information needed to include a pediatric claim are ongoing.
- 5. Some information on pediatric dosing and safety are included in the draft labeling but without a specific pediatric claim.

(Check the appropriate blanks under #2 to indicate whether further data on effectiveness in pediatric patients will be obtained in Phase 4 studies.)

- 6. The proposed claim in the draft labeling is specifically directed toward a pediatric illness, e.g., petit mal seizures, otitis media, JRA, patent ductus.
- 7. The dosage form is expected to be used primarily in the pediatric population.
 - a. A specific pediatric claim is included in the labeling.
 - b. The labeling does not include a specific pediatric claim. Check the appropriate blanks under #2 to indicate whether further data on effectiveness in pediatric patients will be obtained in Phase 4 studies.)

CC: ORIGINAL NDA 20-587
 HFD-150/DIV FILE
 A MARTIN
 LKEIFFER
 DCATTERSON

Consult #536 (HFD-150)

SCLEROSOL

sterile aerosol talc

A review revealed no look-alike/sound-alike conflicts with the proposed trademark and the Committee finds the trademark acceptable. However, the Committee feels that the established name for the product should be talc aerosol since there is no official category for sterile aerosol in the USP.

The Committee has no reason to find the proposed trademark unacceptable.

CDER Labeling and Nomenclature Committee

_____, Chair
7



MAY 29 1997

NDA 20-587

Bryan Corporation
4 Plympton Street
Woburn, MA 01801

Attention: Frank M. Abrano
Chief Executive Officer

Dear Mr. Abrano:

We acknowledge receipt on April 29, 1997 of your April 28, 1997 amendment to your new drug application (NDA) for Sclerosol Intrapleural Aerosol (sterile talc powder).

This amendment contains additional chemistry, microbiology, environmental assessment, and labeling information submitted in response to our August 9, 1996 approvable letter.

We consider this a major amendment under 21 CFR 314.60 of the regulations and it constitutes a full response to our letter. Therefore, the due date under the Prescription Drug User Fee Act of 1992 (PDUFA) is October 29, 1997.

If you have any questions, please contact Debra Catterson, Project Manager, at (301) 827-1544.

Sincerely yours,

5-29-97

Robert J. DeLap, M.D., Ph.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

NDA 20-587

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cc:

Original NDA 20-587
HFD-150/Div. Files
HFD-150/CSO/D. Catterson
HFD-150/AMartin
HFD-150/JBeitz
HFD-150/RBarron
HFD-150/RWood
HFD-150/WSchmidt
HFD-150/PAndrews
HFD-150/ARahman
HFD-150/LKieffer
HFD-150/CGnecco
HFD-805/DHussong
HFD-350/NSager
DISTRICT OFFICE

Duffen
5-29-97

Final by: DCatterson/May 19, 1997/c:\wpfiles\nda's\talc\arespon.ltr

ACKNOWLEDGEMENT (AC)



NDA 20-587

AUG 31 1995

Bryan Corporation
4 Plympton Street
Woburn, MA 01801

Attention: Frank Abrano
Chief Executive Officer

Dear Mr. Abrano:

We have received your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Sterile Aerosol Talc,

Therapeutic Classification: Priority

Date of Application: August 11, 1995

Date of Receipt: August 15, 1995

Our Reference Number: NDA 20-587

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on October 14, 1995 in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations and in accordance with the policy described in the Center for Drug Evaluation and Research Staff Manual Guide CDER 4820.6, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Please request the meeting at least 15 days in advance. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact Debra Catterson, R.Ph., Project Manager, (301) 827-1544.

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The NDA number listed above should be referenced at the top of the first page of any communications concerning this application.

Sincerely yours,

RSI

8-30-95

Robert L. Justice, M.D.

for Acting Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

NDA 20-587

Page 3

cc:

Original NDA 20-587

HFD-150/Division File

HFD-151/DCatterson/8.28.95

R/D init by: DPease/8-30-95

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ACKNOWLEDGEMENT LETTER