APPLICATION NUMBER:
20-452

MICROBIOLOGY REVIEW
Product Quality Microbiology Review  
Review for HFD-150  
26 MAR 2003

NDA: 20-452

Drug Product Name  
Proprietary: Paraplatin  
Non-proprietary: Carboplatin solution  
Drug Product Classification: Anti-neoplastic

Review Number: 2

Subject of this Review  
Submission Date: 11 OCT 2002  
Receipt Date: 15 Oct 2002  
Consult Date: 08 JAN 2003  
Date Assigned for Review: 17 JAN 2003

Submission History (for amendments only)  
Date(s) of Previous Submission(s): 31 MAR 1994  
Date(s) of Previous Micro Review(s): 4 OCT 1994

Applicant/Sponsor  
Name: Bristol-Myers Squibb  
Address: P.O. Box 5400  
Princeton, NJ 08543-5400  
Representative: Noemi C. Guma, Ph.D.  
Telephone: (609) 818-5759

Name of Reviewer: David Hussong

Conclusion: APPROVE
Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: New NDA amendment

2. SUPPLEMENT PROVIDES FOR: Response to deficiencies in review dated 4 October 1994

3. MANUFACTURING SITE: Bristol Caribbean, Inc.
   Mayaguez, PR 00708

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 10 mg/mL solution of 10, 15 and 45 mL volumes in vials containing 50, 150 and 450 mg. The 50 mg product is in a — vial. The 150 mg product is in a — vial. The 450 mg product is in a — vial.

5. METHOD(S) OF STERILIZATION: ———

6. PHARMACOLOGICAL CATEGORY: Anti-neoplastic, cytotoxic

B. SUPPORTING/RELATED DOCUMENTS: DMF ——— (date of update is 3 June 1997).

C. REMARKS: This amendment responds to review comments from 1994. The original NDA described the aqueous form of a lyophilized product (NDA 19-880). The review of the original NDA noted that these were minor deficiencies and could be addressed as Phase 4 commitments.

   The questions shown in the amendment are different from the questions sent in the review. It is not clear where they were altered.

filename: 20-452Rv2.doc
Executive Summary

I. Recommendations

A. Recommendation on Approvability - APPROVE

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – N/A

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature

B. Endorsement Block
   David Hussong/Microbiologist
   Peter Cooney/Microbiology Supervisor

C. CC Block
   cc:
   Original NDA 20-452
   HFD- 150/Division File/NDA 20-452
3 Page(s) Withheld
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

------------------------
David Hussong
3/27/03 10:13:09 AM
MICROBIOLOGIST

Peter Cooney
3/27/03 11:08:35 AM
MICROBIOLOGIST
CONSULTATIVE REVIEW TO HFD-150

DIVISION OF MEDICAL IMAGING, SURGICAL,
and DENTAL DRUG PRODUCTS; HFD-160

Microbiologist’s Review #1
4 October 1994

A. 1. NDA 20-452

APPLICANT

Bristol-Myers Squibb Co.
Pharmaceutical Research Institute
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06492-7660

2. PRODUCT NAMES: Paraplatin® — Carboplatin —

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: A 10 mg/mL solution of 10, 15 and 45 cc volumes in vial presentations containing 50, 150 and 450 mg (respectively) for dilution into a parenteral fluid and intravenous infusion over a 6 to 8 hour period. Dose rates are based on patient surface area.

4. METHOD(S) OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY: Anti-neoplastic

6. DRUG PRIORITY CLASSIFICATION: 3P

B. 1. DATE OF INITIAL SUBMISSION: 31 March 1994

2. DATE OF AMENDMENTS: 31 March 1994 and 7 April 1994


C. REMARKS: The product represents an aqueous presentation of the same drug for a lyophilized dosage form (NDA 19-880, approved 3 March 89). The original submission for NDA 19-880 manufactured on these filling lines is Taxol (NDA 20-262) which was reviewed in December 1992 (Microbiologist’s Review #1) and August 1993 (Microbiologist’s Review #2). The lyophilized product contains equal quantities (w/w) of mannitol to drug substance, whereas the aqueous product contains only drug substance and water.
The 2 volumes of Amendment 1 contain a summary and 6 Attachments. These address of stoppers and vials, of filling equipment, and media fills.

D. CONCLUSIONS: The submission is not recommended for approval. However, issues described in the Microbiologist's Letter to the Applicant may be addressed post-approval, pending a commitment by the applicant. For additional details, refer to section "E. Review Notes".

David Hussong, Ph.D.

cc:
Original NDA 20-452
HFD 160/Consult File
HFD 150/Division File
HFD 150/CSO/D.Daproza
HFD 150/Chemist/E.Tolgyesi
drafted by: D.Hussong, 10/04/94
R/D initialed by: P.Cooney, 10/05/94
9 Page(s) Withheld