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RESEARCH**

APPLICATION NUMBER:
201195Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

05 October 2010

NDA: 201-195/N-000

Drug Product Name

Proprietary:

N/A.

Non-proprietary:

Docetaxel Injection.

Review Number:

1.

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
21 DEC 2009	22 DEC 2009	03 FEB 2010	04 FEB 2010
20 SEP 2010	21 SEP 2010	N/A	N/A

Applicant/Sponsor

Name:

Accord Healthcare, Inc.

Address:

1009 Slater Rd.

Suite 210-B

Durham, NC 27703.

Representative:

Samir Mehta

Telephone:

1-919-941-7878

Name of Reviewer:

John W. Metcalfe, Ph.D.

Conclusion:

Recommend approval.

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** An original NDA.
 - 2. SUBMISSION PROVIDES FOR:** A 505(b)(2) drug.
 - 3. MANUFACTURING SITE:**
Intas Pharmaceuticals Limited.
Plot No. 457,458
Village-Matoda,
Bavla Road, Ta. Sanand,
Dist. Ahmedabad-382 210
Gujarat, India.
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Solution for Injection.
 - Intravenous Injection.
 - 20 mg/0.5 mL and 80 mg/2.0 mL.
 - 5. METHOD(S) OF STERILIZATION:**
 - Drug Product: (b) (4)
 - Diluent: (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** The subject drug product is indicated for the treatment of cancer.
- B. SUPPORTING/RELATED DOCUMENTS:** None.

C. REMARKS:

The NDA is submitted in paper. Volumes 1 through 9 of Module 3, along with one jacket each of Modules 1 and 2 were provided for review.

An Initial Quality Assessment was entered into DARRTS by ONDQA on 25 February 2010. The IQA does not identify any critical review issues pertaining specifically to Product Quality Microbiology.

On 02 September 2010, this reviewer forwarded the following Information Request to the OND Project Manager for dissemination to the applicant:

A microbiology review of NDA 201-195 is in progress.

Reviewer's Comment

The drug product release specification provides a limit for bacterial endotoxins of NMT (b) (4) while the diluent release specification includes a limit for

this attribute of NMT (b) (4) Preparation of a dose of 100 mg/m² for a patient with a BSA of 1.8m² would necessitate the use of 9 product vials and 9 diluent vials. If both the product and diluent contain the maximum allowable limit for bacterial endotoxins, a total load of (b) (4) will be delivered to the patient. An endotoxin load of (b) (4) exceeds the USP<85> allowable limit of 350 EU per hour.

- Lower the diluent limit for bacterial endotoxins to provide an individual with a BSA of 1.8m² a margin of safety regarding bacterial endotoxins. Reference is made to USP<85> which states the following regarding the establishment of endotoxin limits:
“For formulations (usually anticancer products) administered on a per square meter body surface, the formula is K/M, where K = 5 EU/kg and M is the (maximum dose/m²/hour x 1.80 m²)/70 Kg.”

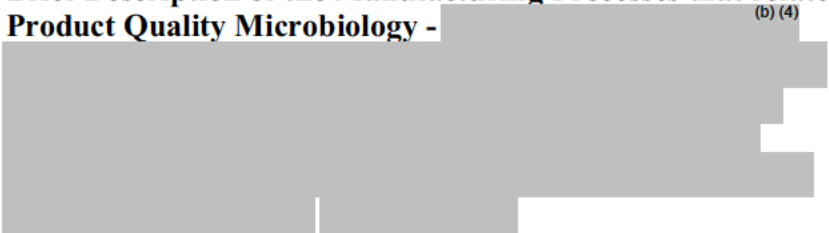
The applicant amended the NDA on 20 September 2010 addressing the above point. The amended diluent endotoxin limit is summarized and reviewed in Section P.5.2 of this review.

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 201-195/N-000 is recommended for approval on the basis of issues pertaining to product quality microbiology.
- B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – Not applicable.

II. Summary of Microbiology Assessments

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -** (b) (4)

- B. **Brief Description of Microbiology Deficiencies** – There are no microbiology deficiencies identified.
- C. **Assessment of Risk Due to Microbiology Deficiencies** – Not applicable.

III. Administrative

- A. **Reviewer's Signature** _____
John W. Metcalfe, Ph.D.
- B. **Endorsement Block** _____
Bryan S. Riley, Ph.D.
- C. **CC Block**
N/A

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

/s/

JOHN W METCALFE
10/05/2010

BRYAN S RILEY
10/05/2010
I concur.