

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203551Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

10/17/2012

NDA: 203551

Drug Product Name

Proprietary:

Non-proprietary: Docetaxel Injection Concentrate, 20 mg/ml

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
3/14/2012	3/14/2012	4/02/2012	4/04/2012
7/27/2012	7/27/2012	N/A	N/A
10/09/2012	10/09/2012	N/A	N/A

Submission History (for amendments only)

None

Applicant/Sponsor

Name: Actavis Inc

Address: 60 Columbia Rd, Building B, Morristown, NJ 07960

Telephone: 908 659 2317

Representative: Donald H. Chmielewski, Lachman Consultant Services

Telephone: 516 222 6222

Name of Reviewer: Steven P. Donald, M.S.

Conclusion: Approval recommended

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original NDA
2. **SUBMISSION PROVIDES FOR:** Manufacture and marketing of a sterile drug product.
3. **MANUFACTURING SITE:**
S.C. SINDAN-PHARMA S.R.L.
11 Ion Mihalache Blvd
Bucharest 011171, Romania
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 20 mg/ml; 1 ml, 4 ml and 7 ml fills into 5 ml, 8 ml and 11 ml glass vials.
5. **METHOD(S) OF STERILIZATION:** (b)(4)
6. **PHARMACOLOGICAL CATEGORY:** chemotherapeutic

B. **SUPPORTING/RELATED DOCUMENTS:**

DMF (b)(4) from (b)(4) for the depyrogenation of the rubber stoppers. The LOA date is 12/21/2010.

DMF (b)(4) for the (b)(4) washing process in record #713 was found adequate in review (b)(4) mic14.doc, dated 8/5/2010.

DMF review (b)(4) mic18.doc, dated 9/01/2011, covers Annual Report # 5 (additional information provided by the DMF holder) to Record #713 pertaining to the (b)(4) washing and drying process for the depyrogenation of (b)(4) (b)(4) closures.

C. **REMARKS:**

An information request dated 5/22/2012 was provided to the applicant. A response was received on 7/27/2012 providing responses to specific questions regarding product quality microbiology. Responses are provided in this review below each deficiency. Additionally, in the same submission, the applicant provides a gratuitous amendment for the addition of an alternate (b)(4). See Sections 3.2.P.3.2 and 3.2.P.3.5 for the added information. Another information request dated 8/07/2012 was sent to the applicant after review of the gratuitous amendment and IR response of 7/27/2012. The response to the 8/07/2012 information request was dated 10/5/2012 with a submission and received date of 10/09/2012.

filename: N203551R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability –**
NDA 203551 is recommended for approval from the standpoint of product quality microbiology.
- 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 -** The drug product will be (b)(4) processed.
- B. Brief Description of Microbiology Deficiencies –** No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies -**
N/A

III. Administrative

- A. Reviewer's Signature** _____
Steven P. Donald, M.S.
- B. Endorsement Block**
Team Leader: Bryan Riley, Ph.D.
- C. CC Block**
N/A

35 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

STEVEN P DONALD
10/31/2012

BRYAN S RILEY
11/01/2012
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 203551

Applicant: Actavis Inc.

Letter Date: 3/14/2012

Drug Name: Docetaxel

NDA Type: 505 (b)(2)

Stamp Date: 3/14/2012

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		e-CTD Format
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		3.2.p.3.4
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		3.2.P.3.5
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		CCI information supplied on 4/11/2012 in response to an Information request sent on 4/10/2012.
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		3.2.P.5.1
7	Has the applicant submitted the results of analytical method verification studies?	X		Sterility testing validation data are present in section 3.2.P.5.3.7 but not clear if they are adequate
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			N/A
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: An information request was sent to the sponsor, through the project manager, on 4/10/2012. A response from the sponsor was provided on 4/11/2012 by email. Following are comments and responses:

Comments to be forwarded to the Sponsor:

Please provide Container/Closure Integrity studies for all configurations of the subject drug product. It is stated in Pharmaceutical Development that these studies are provided in 3.2.P.3.5.5, however this section cannot be located within the submission.

Response:

The applicant provided a revised 3.2.P.3.5 section (32P5Process Evalutaion.pdf) that included container/closure integrity studies using the same vials that are used for the proposed drug product. This reviewer requested that this information be officially submitted by the applicant to the NDA application.

Acceptable

Reviewing Microbiologist: Steven P. Donald, M.S.

Date: 4/09/2012

Microbiology Team Leader; Bryan Riley, Ph.D.

Date: 4/09/2012

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

/s/

STEVEN P DONALD
04/17/2012

BRYAN S RILEY
04/17/2012
I concur.