

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
201023

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

08-JUN-2010

NDA 201023/N-000

Drug Product Name

Proprietary: Jevtana®

Non-proprietary: Cabazitaxel

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
08-JUN-2010	08-JUN-2010	N/A	N/A
25-MAY-2010	25-MAY-2010	N/A	N/A
21-MAY-2010	21-MAY-2010	N/A	N/A
24-FEB-2010	24-FEB-2010	15-MAR-2010	16-MAR-2010

Applicant/Sponsor

Name: Sanofi Aventis

Address: 55 Corporate Drive
Bridgewater, NJ 08807

Representative: Linda Gustavson, Ph.D.

Telephone: 908-304-6221

Name of Reviewer: Steven Fong, Ph.D.

Conclusion: CMC-Microbiology recommends APPROVE.

Product Quality Microbiology Data Sheet

- A. 1. TYPE OF SUBMISSION:** Original NDA.
- 2. SUBMISSION PROVIDES FOR:** New drug product.
- 3. MANUFACTURING SITE:**
Aventis Pharma, Dagenham
Rainham Road South
Dagenham, Essex RM 107XS
United Kingdom
- 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Intravenous solution for infusion.
 - Provided as a kit containing two vials:
 - Cabazitaxel concentrate for solution for infusion (CCSI), 60 mg/1.5 mL.
 - Cabazitaxel solvent (CS), 5.7 mL 13% w/w alcohol. The volume includes a (b) (4) overfill. Only (b) (4) is used for dilution of CCSI.
 - (b) (4) from the CS vial is mixed with the CCSI vial contents to form a 10 mg/mL intermediate premix.
 - Premix is diluted with 0.9% sodium chloride or 5% dextrose in an infusion bag.
- 5. METHOD(S) OF STERILIZATION:**
- CCSI is sterilized by (b) (4)
 - CS is sterilized by (b) (4)
- 6. PHARMACOLOGICAL CATEGORY:** Prostate cancer therapeutic.
- B. SUPPORTING/RELATED DOCUMENTS:** None.
- C. REMARKS:**
- The application was provided in a rolling submission format. The original submission was submitted 18-DEC-2009 and contained non-clinical information only. CMC information was submitted 24-FEB-2010 (amendment 1, supporting document 2) in eCTD format.
 - The application proposes a promising therapy for metastatic prostate cancer. On 09-NOV-2009 the submission was granted Fast Track status.
 - On 11-MAY-2010 an IR was submitted requesting details regarding the bacterial ingress test used to assess container-closure integrity, and the method
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and method validation for depyrogenation of the rubber stoppers used for product closure. An amendment response (sponsor submission 14) was received on 21-MAY-2010.

- On 18-MAY-2010 a second IR was submitted requesting information regarding the (b) (4), the endotoxin testing method, the environmental monitoring action limits, and (b) (4) (b) (4) validation. An amendment response (sponsor submission 17) was received on 25-MAY-2010.
- On 04-JUN-2010 the reviewer placed a phone call to Sanofi-Aventis regulatory affairs representative Linda Gustavson regarding the stability data presented in support of the proposed CCSI shelf life. On the same day a return phone call was received from Sanofi-Aventis regulatory affairs CMC specialist Zareen Ahmed clarifying that the information was present in CCSI submission section 3.2.P.8.3, Table 1.
- On 07-JUN-2010 an IR was sent to the sponsor requesting data supporting the proposed (b) (4). On 08-JUN-2010 an amendment response was received that contained the requested data.
- The application presented the manufacturing information for CCSI and CS in two separate sections. In this review these are referred to, respectively, as the CCSI and the CS submission sections.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – Recommended for approval from a microbiology quality standpoint.
- 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 - CCSI** (b) (4)
 15 mL glass vials that are sealed with 13 mm grey (b) (4) rubber stoppers and aluminum overseals. CS (b) (4) and (b) (4) for CCSI: 15 mL glass vials sealed with 13 mm grey (b) (4) rubber stoppers and aluminum overseals. The CS vials are sterilized (b) (4) (b) (4)
- B. Brief Description of Microbiology Deficiencies** – No deficiencies identified.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Minimal risk.

III. Administrative

- A. Reviewer’s Signature** _____
 Steven Fong, Ph.D., Microbiology Reviewer
- B. Endorsement Block** _____
 Bryan Riley, Ph.D.
 Senior Microbiology Reviewer
- C. CC Block** N/A

26 pages of Microbiology has been withheld in full immediately following this page as B4 CCI/TS

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201023	ORIG-1	SANOFI AVENTIS SPA	CABAZITAXEL (XRP6258)

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

/s/

STEVEN E FONG

06/08/2010

Recommended for approval from a microbiology quality standpoint.

BRYAN S RILEY

06/08/2010

I concur.