

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**201023s000**

**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**

<b>Submit</b>	<b>Received</b>	<b>Review Request</b>	<b>Assigned to Reviewer</b>
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
-

---

and method validation for [REDACTED]<sup>(b) (4)</sup> 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 [REDACTED]<sup>(b) (4)</sup>, the endotoxin testing method, the environmental monitoring action limits, and [REDACTED]<sup>(b) (4)</sup> 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 [REDACTED]<sup>(b) (4)</sup>. 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.

**filename:** N201023r1.doc

---

## **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** is (b) (4) 15 mL glass vials that are sealed with 13 mm grey (b) (4) rubber stoppers and aluminum overseals. CS is (b) (4) filled into the same container-closure system used for CCSI: 15 mL glass vials sealed with 13 mm grey (b) (4) rubber stoppers and aluminum overseals. The CS vials are (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 Have Been Withheld In Full As b4(CCI/TS) Immediately Following This Page

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.