

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

202799Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

27 January 2012

NDA: 202-799/N000

Drug Product Name

Proprietary: Omontye (proposed)

Non-proprietary: peginesatide injection

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
23 May 2011	27 May 2011	06 June 2011	Transferred from S. Fong to current reviewer on 25 October 2011
18 July 2011	18 July 2011	NA	NA

Submission History (for amendments only) – NA

Applicant/Sponsor

Name: Affymax, Inc.

Address: 4001 Miranda Ave.
Palo Alto, CA 94304

Representative: Anne-Marie Duliege, MD, MS,
Chief Medical Officer

Telephone: (650) 812-8727

Name of Reviewer: Denise A. Miller

Conclusion: Approve

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original Application
2. **SUBMISSION PROVIDES FOR:** The submission is for the manufacture of a sterile drug solution for injection in multiple strengths with three presentations; single-dose vials, multi-dose vials and single-dose prefilled syringes.
3. **MANUFACTURING SITE:**
Single-dose vials (SDV) and Multi-dose vials (MDV)
Takeda Pharmaceutical Company
4720 Takeda Mitsui Hikariki Yamaguchi
743-8502, Japan
FEI: 3002808306

Pre-filled syringe (PFS)

(b) (4)

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
Dosage Form: Sterile solution for injection
Route of Administration: Intravenous and subcutaneous
Strength/Potency:
Single-dose vials: 2, 3, 4, 5, and 6 mg/vial
Pre-filled syringes: 1, 2, 3, 4, 5, and 6 mg/syringe
Multi-dose vials: 10 and 20 mg/vial

5. **METHOD(S) OF STERILIZATION:** (b) (4)

6. **PHARMACOLOGICAL CATEGORY:** Treatment of anemia associated with chronic renal failure in adult patients on dialysis

B. **SUPPORTING/RELATED DOCUMENTS:**

DMF (b) (4) Drug Master File LOA 13 September 2010

(b) (4)

Report H080070 submitted September 17, 2009. Report H080070 was reviewed in 501mic12.doc, 501mic12a1.doc and 501mic12a2.doc. The deficiencies

in Report H080070 noted in the first two reviews were addressed by the DMF holder and found adequate in 501mic12a2.doc. The remaining deficiency noted in 501mic12a2.doc is not applicable to the proposed (b) (4) and therefore this DMF is adequate for this application

(b) (4)
submitted September 10, 2010. The audit report was reviewed by NDMS in D00501_2010Sept_13A1.doc and found to be adequate.

DMF (b) (4) LOA 10 August 2010 (b) (4)
(b) (4) for (b) (4)
of October 06, 2008. This submission was reviewed by OGD on 05 Jan 2009 and 5 April 2011; both reviews determined that the DMF was adequate.

C. REMARKS:

- 1) Application was e-CTD format.
- 2) An Information Request (IR) was sent during the filing review requesting information on the container closure integrity studies for the pre-filled syringes and the preservative effectiveness studies for the multidose vials. A response was received on July 18, 2011 from the sponsor.

filename: N202799R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - Recommend to approve from a quality microbiology standpoint.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - NA

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – The drug product is ^{(b) (4)} in single-use vials, multi-use vials, and pre-filled single-use syringes.
- B. Brief Description of Microbiology Deficiencies** – No quality microbiology deficiencies identified from the information submitted. There is a comment to be forwarded to the sponsor regarding the bioburden sampling point.
- C. Assessment of Risk Due to Microbiology Deficiencies** - NA

III. Administrative

- A. Reviewer's Signature** _____
Denise A. Miller
Microbiologist, NDMS
- B. Endorsement Block** _____
Stephen E. Langille, Ph.D.
Senior Microbiologist, NDMS
- C. CC Block**
N/A

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/s/

DENISE A MILLER
02/01/2012

STEPHEN E LANGILLE
02/01/2012

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 202-799/N-000 Applicant: Affymax, Inc. Submit Date: 23-MAY-2011
Drug Name: AF37702 Injection NDA Type: Original NDA Receipt Date: 27-MAY-2011

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		Submission provided electronically in 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		Sections 2.3.P and 3.2.P.3.3
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		Section 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	Submission was provided in English.
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		Preservative effectiveness described in Section 3.2.P.2.6. Container closure integrity for single and multi-dose vials described in section 3.2.P.2.7. Integrity of pre-filled syringes described in Section 3.2.P.2.4.4 See also Additional Comments
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Sections 2.3.P.5.1 and 3.2.P.5.1.
7	Has the applicant submitted the results of analytical method verification studies?	X		Sections 2.3.P.5.1.4, 2.3.P.5.1.5, 3.2.P.5.2, and 3.2.P.5.3.
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	N/A	N/A	Pre-submission microbiology quality requests were not made.
9	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: AF37702 Injection will be provided in single dose vials and pre-filled syringes (PFS's) containing 2 mg/0.5 mL, 3 mg/0.5 mL, 4 mg/0.5 mL, 5 mg/0.5 mL, and 6 mg/0.5 mL of drug product, and multi-dose vials containing 10 mg/1 mL and 20 mg/2 mL of drug product. The formulation in the multi-dose vials varies from the single dose and PFS

formulation in containing (b) (4) phenol (b) (4) The product for all dose formats is manufactured using (b) (4)

On 14-Jul-2011 an IR was sent to the Applicant requesting validation procedures, acceptance criteria and data sets for preservative efficacy and PFS container closure integrity. On 19-JUL-2011 an Amendment response was received that contained the requested preservative efficacy validation studies. The latter were presented in a revision of Submission Section 3.2.P.2.5, *Microbiological Attributes AF37702 Injection Multiple Dose Vial (MDV)*. The Amendment additionally clarified that container closure validation information for the PFS was provided in Submission Section 3.2.P.2.4.4.

Steven Fong, Ph.D.
Review Microbiologist

19-JUL-2011

John Metcalfe, Ph.D.
Senior Review Microbiologist

19-JUL-2011

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/s/

STEVEN E FONG

07/19/2011

The Application is recommended for filing from a microbiology quality standpoint.

JOHN W METCALFE

07/19/2011

I concur.