CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208471Orig1s000

MICROBIOLOGY/VIROLOGY REVIEW(S)

Product Quality Microbiology Review

29 JUL 2013

NDA: 204-961

Drug Product Name
Proprietary: (b) (4)
Non-proprietary: Lixisenatide

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
19 DEC 2012	20 DEC 2012	26 DEC 2012	04 JAN 2013
24 MAY 2013	24 MAY 2013	N/A	N/A
02 JUL 2013	02 JUL 2013	N/A	N/A

Applicant/Sponsor
Name: Sanofi-Aventis US, LLC
Address: 55 Corporate Drive
Bridgewater, NJ 08807
Representative: Ayse Baker
Telephone: 908-981-4799

Name of Reviewer: Jessica G. Cole, PhD

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original 505(b)(1) NDA

2. SUBMISSION PROVIDES FOR: New molecular entity

3. MANUFACTURING SITE: [redacted] (b) (4)

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:

- Sterile, preserved solution for subcutaneous injection
- 3 mL [redacted] (b) (4) cartridge in a multiple dose pen injector
- 0.05 mg/mL and 0.1 mg/mL with a proposed dose of 10 µg or 20 µg once daily

5. METHOD(S) OF STERILIZATION: [redacted] (b) (4) processing

6. PHARMACOLOGICAL CATEGORY: Improved glycemic control in adults with type 2 diabetes

B. SUPPORTING/RELATED DOCUMENTS: Microbiology review of DMF [redacted] (b) (4) dated 29 July 2013.

C. REMARKS: The NDA is entirely in the eCTD format. The following information request was sent to the ONDQA PM on 17 April 2013. A response was received from the applicant on 24 May 2013. The responses have been incorporated into the relevant sections of this review.

Microbiology Comment:
Please provide the following information or a reference to its location in the relevant submission.

1. Provide the incubation temperature and concentration of *Serratia marcescens* in the microbial ingress container-closure studies. Provide the bacterial concentration at the start and end of the 14 day incubation period.
2. Provide a justification for collecting the bioburden sample [redacted] (b) (4) for process variant [redacted] (b) (4) [redacted] (b) (4)
3. Provide the following details on the bacterial retention studies for the [redacted] (b) (4) proposed for commercial use:
   a. [redacted] (b) (4)
   b.

c. [redacted] (b) (4)

4. Provide the incubation conditions used for the *Geobacillus stearothermophilus* biological indicators used in validation studies for [redacted] (b) (4)
5. Describe the qualification/requalification plan for modules [redacted] (b) (4) management system. Address the following points:
   a. Provide an explanation for the minimum lethality in module [redacted] (b) (4)
   b. Indicate whether Table 84 (Module 3.2.P.3.5.4.1.10.2.2) shows initial qualification or requalification runs.
   c. Provide a justification for not requalifying the [redacted] (b) (4) runs since 2009.
6. Provide a more detailed description of the monitoring points for the [redacted] (b) (4) studies. Clarify how the following statement relates to Figures 18 and 19 (Module 3.2.P.3.5.4.2.5.2) [redacted] (b) (4)
7. Provide the following information for the media fills submitted for [redacted] (b) (4). The number of units filled, the number of units rejected (with a brief rationale for the rejection), the number of units incubated, and the total fill duration (in hours).
8. Provide the following information on the dye ingress container-closure studies proposed for use in the stability program.
   a. The number of units tested at each time point in stability
   b. The method by which dye ingress will be assessed (i.e., visual inspection or spectrophotometric)
   c. The sensitivity of the method
   d. A description of the positive and negative controls

For a description of the information that should be submitted in an NDA please refer to the following Guidance document:
Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products
(http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072171.pdf)

The following information request was sent to the applicant on 07 June 2013 and a response was received on 02 July 2013. The responses have been incorporated into the relevant sections of this review.

Microbiology Comment:

The filter validation studies described to date [redacted] (b) (4)

For more information, we refer to PDA Technical Report 26 Filtration [redacted] (b) (4)

filename: N204961R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for Approval.

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 – The drug product is a preserved, multi-dose product that is (b) (4) processed.

B. Brief Description of Microbiology Deficiencies – Not applicable.

C. Assessment of Risk Due to Microbiology Deficiencies – Not applicable.

D. Contains Potential Precedent Decision(s)- ☐ **Yes** ☒ **No**

III. Administrative

A. Reviewer's Signature _____
Jessica G. Cole, PhD

B. Endorsement Block _____
Bryan Riley, PhD
Microbiology Team Leader

C. CC Block
In DARRTS

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

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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/

JESSICA COLE
07/30/2013

BRYAN S RILEY
07/30/2013
I concur.