DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

CBER REGULATORY REVIEW MEMORANDUM

Date 18 June, 2018

From Hyesuk Kong, Ph. D.
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Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To Biologics License Application Submission Tracking Number # 125661/0

Subject BLA: Review of Sterility, Bacterial Endotoxin Test Method Qualification for JIVI® (Recombinant B-domain deleted human coagulation factor VIII conjugated with polyethylene glycol)

Through James L. Kenney, D.Sc., Chief, LMIVTS
Maryna Eichelberger, Ph. D., Director, DBSQC

Applicant Bayer Healthcare, LLC (Bayer)

Product JIVI® (Antihemophilic Factor [Recombinant], PEGylated)

Biologics License Application (BLA) Submission Tracking Number (STN) 125661/0

Submission Received by CBER 30 August, 2017

Review Completed 18 June, 2018

Material Reviewed

Method qualifications for: 1) bioburden; 2) sterility; and 3) bacterial endotoxin test (BET) using (b) (4) performed on JIVI®; and the responses to CBER's Information Requests (IRs), received 13 November and 1 December of 2017, and 31 January and 6 February of 2018, were reviewed.

Executive Summary

After a thorough review of this BLA and the responses to CBER's IRs (Amendments 125661/0/6, 125661/0/9, 125661/0/14 and 125661/0/16), this reviewer finds the bioburden, sterility, (b) (4) methods were qualified in accordance with (b) (4) respectively by demonstrating JIVI® is suitable for the intended test methods.

Background

On 30 August, 2017, Bayer submitted this BLA for their antihemophilic factor, PEGylated B-domain deleted recombinant human factor VIII (rFVIII) with a 60 kilodalton polyethylene-glycol-maleimide conjugated to the protein. It is indicated for use in previously treated adults and adolescents (12 years of age and older) with hemophilia A (congenital factor VIII deficiency) for 1) on-demand treatment and control of bleeding episodes; 2) perioperative management of bleeding; and 3) routine prophylaxis to reduce the frequency of bleeding episodes.

JIVI® is formulated as a sterile, non-pyrogenic, white to slightly yellow solid, lyophilized powder for reconstitution with water as diluent for intravenous administration. JIVI® is available as a lyophilized powder in single use glass vials of (b) (4) 500, 1000, 2000, or 3000 international units (IU) in 2.5 mL fill size. After reconstitution with 2.5 mL sterile water for injection, the solution appears as a clear and colorless liquid, free from visible particles.

The DBSQC reviews BLAs and their supplements to ensure analytical methods are appropriate, properly validated and the product matrix is suitable for the intended test method. DBSQC also reviews endotoxin release specifications to ensure they reflect process capability and meet regulatory compliance. These review activities support DBSQC's lot-release mission, which is the confirmatory testing of submitted product samples and the review of manufacturers' lot-release protocols to ensure biological products are released according to licensed test methods and product specifications. Therefore, this review will focus on the method qualifications for Bayer's bioburden, sterility, and endotoxin test methods performed on the JIVI® to determine if they were appropriately qualified to indicate if its matrix is suitable for these intended test methods.

Review

Bioburden Test Qualification (b) (4)

The bioburden qualification test (b) (4)

(b) (4) and the test results indicate the matrix is suitable for the intended test method.

Sterility Test Qualification for Drug Product (DP)

The JIVI® DP was qualified using the (b) (4)

Bacterial Endotoxin Test Method Qualification for DP

Bayer qualified their (b) (4) method for their JIVI® DP at (b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

CBER performed licensing support bacterial endotoxin testing using a (b) (4) . Bayer's qualification report – as reviewed above – supports CBER's licensing support BET results; CBER's licensing support test result memo is included in the STN file. The test samples showed acceptable (b) (4) , as CBER's (b) (4) results by CBER and Bayer were within Bayer's proposed release specification and CBER's results are comparable to Bayer's, as reported in their information request response (Amendment: 125661/0.16).

Conclusions

After a thorough review of this BLA and the responses to CBER's IR, this reviewer finds the Bayer's JIVI® matrix is suitable for testing using their proposed bioburden, sterility and bacterial endotoxin test methods, as they were qualified and performed in accordance with (b) (4) respectively. Therefore, this reviewer finds these methods acceptable for their intended purpose and recommends their approval.