DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

# CBER REGULATORY REVIEW MEMORANDUM

**Date** 20 December, 2016

**From** Simleen Kaur, M.S., Team Lead
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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 # 125612/0

**Subject** BLA: Review of Bioburden, Sterility, Endotoxin and General Safety Test Methods for Fibryna®, Human Fibrinogen

**Through** James L. Kenney, D.Sc., Chief, LMIVTS
William M. McCormick, Ph.D., Director, DBSQC

**Applicant** Octapharma

**Product** Fibryna®, Human Fibrinogen

**Biologics License Application (BLA) Submission Tracking Number (STN)** 125612/0

**Submission Received by CBER** 9 June, 2016

**Review Completed** 20 December, 2016

## Material Reviewed

Method qualifications for: 1) sterility; and 2) endotoxin tests performed on Fibryna®. In addition, procedures for general safety test and information request response received 3 October of 2016 were reviewed.

## Executive Summary

After a thorough review of this BLA, this reviewer finds the sterility, and endotoxin test methods were qualified in accordance with (b) (4) , respectively. In addition, the general safety test is being performed in accordance to 21 CFR 610.11.

## Background

On 9 June, 2016, Octapharma submitted this BLA for Fibryna® indicated for treatment of acute bleeding episodes (b) (4) in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. Fibryna® is a plasma-derived, highly purified concentrate of fibrinogen for intravenous application, provided as a lyophilized powder containing 20mg of human fibrinogen as an active ingredient.

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 release specifications for microbial and endotoxin testing to ensure they reflect process capability and meet regulatory compliance. These review activities support DBSQC's lot-release mission: the confirmatory testing of submitted product samples; 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 following method qualifications for Octapharma's sterility and endotoxin test methods to ensure the product matrix is suitable for these intended test methods and the review of general safety test procedure to ensure it is compliant with 21 CFR 610.11.

**Review**

Sterility Test Qualification for Drug Product

Octapharma qualified their Fibryna® Drug Product (DP) matrix using the (b) (4)

(b) (4)

(b) (4)

(b) (4) Method Qualification for Drug Product (DP)

Octapharma qualified their (b) (4) method for Fibryna® DP to verify their product matrix was suitable for the intended test method in accordance with (b) (4) .

Octapharma tested for a suitable test dilution using (b) (4) lot of DP (b) (4)

(b) (4)

Octapharma submitted the endotoxin results for several DP lots, which met their endotoxin test specification of (b) (4). CBER finds these proposed specifications acceptable.

General Safety for DP

CBER reviewed the SOPs, 137SOP028/01: "Test for General Safety according to 21 CFR" provided in the original submission. The SOP was found to be in accordance with 21CFR 610.11, General Safety.

Octapharma submitted the general safety test results for several clinical and commercial batches and and results were found to be accordance with 21 CFR 610.11 indicating an absence of harmful extraneous contaminants in their final container product matrix.

**Conclusions**

After a thorough review of the information submitted in this BLA, this reviewer finds Octapharma's Fibryna® DP matrix is suitable for testing using their sterility and endotoxin testing methods, as these tests were qualified and performed in accordance with (b) (4), respectively. In addition, general safety test on the final container matrix is performed in accordance with 21 CFR 610.11. Therefore, this reviewer finds these methods acceptable for their intended purpose.