DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

MEMORANDUM FOR RECORD 24 February, 2017

To STN # 125612/0

From Hyesuk Kong, Ph. D.
Laboratory of Microbiology, *In-vivo* Testing & Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)

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

Cc Thomas Maruna, RPM, OTAT
Peng Ze, Chair, BLA Review Committee

Subject CBER In-support (b) (4) Endotoxin Test Results on Fibryna®, Human Fibrinogen

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The Division of Biological Standards and Quality Control's Laboratory of Microbiology, *In-vivo* Testing and Standards tested five lots of Fibryna® Final Drug Product for (b) (4) endotoxin using the (b) (4) test method, as Octapharma Pharmazeutika Produktionsges,M.B.H. (Octapharma) is requesting the approval of this method in their license application. The (b) (4) endotoxin results obtained by CBER along with those of Octapharma are listed below:

(b) (4) **Results**

Lot Number	Test Dilution	CBER (b) (4)	Test Dilution	CBER (b) (4)	CBER Results ((b) (4))	Octapharma's Results ((b) (4))	Proposed Specification ((b) (4))
A423A3472	(b) (4)	(b) (4)	(b) (4)	(b) (4)	0.1	< 0.1	(b) (4)
A441A3474					< 0.1	< 0.1	
A425A3471					< 0.1	< 0.1	
A440A3472					0.1	< 0.1	
A433A3473					< 0.1	0.1	

(b) (4)

CBER performed licensing support testing for the above lots at test dilution of (b) (4) and (b) (4) following the Octapharma's analytical method validation report (000VAL162FC 34x IP1334x /01 rep) and their lot release protocols (LRPs) submitted to CBER. These five test samples showed no (b) (4) (acceptance criteria (b) (4)) for the (b) (4) and (b) (4) test dilutions, respectively. The (b) (4) endotoxin

results by CBER and Octapharma were within their proposed specification and these results are comparable to the values reported in Octapharma's LRPs.

Note: Octapharma had valid results using the (b) (4) sample testing dilution, as selected in their method qualification report. However, the results as indicated in their LRPs submitted to CBER were generated using a sample testing dilution of (b) (4). CBER sent an information request (IR) to Octapharma on 6 February, 2017, requesting explanation why the (b) (4) dilution was used for testing, which CBER agrees represent a more appropriate dilution to evaluate sample, compared to the (b) (4) test dilution. Based on the review of Octapharma's IR response (Amendment: 125612/0/34), CBER finds Octapharma's proposed (b) (4) sample testing dilution as a routine release testing acceptable.