



MEMORANDUM FOR RECORD

To STN # 125640/0

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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)

Through James L. Kenney, D.Sc., Acting Director, DBSQC/OCBQ/CBER/FDA

Cc Yu Do, RPM, OTAT
Natalya Ananyeva, Chair, BLA Review Committee

Subject CBER In-support Bacterial Endotoxin Test Results on Fibrin Sealant (Human)

The Division of Biological Standards and Quality Control’s Laboratory of Microbiology, *In-vivo* Testing and Standards tested two lots of Fibrin Sealant (i.e., Fibrinogen and Thrombin components) Final Drug Product for bacterial endotoxin using the (b) (4) test method; as Instituto Grifols, S.A.(Grifols) is requesting the approval of this method in their license application. The bacterial endotoxin results obtained by CBER along with those of Grifols are listed below:

Component	(b) (4) * ¹ Results							
	Fibrinogen				Thrombin			
Lot Number	Test Dilution	% Spike Recovery	CBER Results (IU/mL)	Grifols’ Results (IU/mL)* ²	Test Dilution	% Spike Recovery	CBER Results (IU/mL)	Grifols’ Results (IU/mL)* ²
B4YBB00021	(b) (4)	146	< 0.5	< 0.5	1:1000	110	< 5.0	< 0.1
IBND6L3MPI	(b) (4)	128	< 0.5	< 0.5	1:1000	103	< 5.0	< 0.1

*¹ CBER used (b) (4) Test Kit; where Grifols used (b) (4) reagent kit

*² The proposed Bacterial Endotoxin Specification is (b) (4) for both Fibrinogen and Thrombin components.

For fibrinogen, two test samples were tested at a dilution of (b) (4), following Grifols’ analytical method validation report (IG_IVMA-000168_ING) and their testing procedure (IG_MA-000011G_ING) submitted to CBER, showed no inhibition or enhancement as the BET spike recoveries for the positive product control (PPC) were 146 and 128% (acceptance criteria (b) (4)). The BET results obtained by CBER and Grifols for the Fibrinogen lots are listed above and meet their release specification.

For thrombin, CBER experienced invalid PPC recoveries for the above lots at test dilution of (b) (4) following the Grifols’ analytical method validation report (IG_IVMA-000185_ING). CBER re-qualified Grifols’ thrombin lot samples for CBER’s (b) (4)-BET method, due to testing differences observed between different (b) (4) testing kits. CBER’s method was qualified using a sample testing dilution of 1:1000, which was within maximum valid dilution (b) (4). The bacterial endotoxin results for Thrombin component by CBER and Grifols were within their proposed specification.