



CBER REGULATORY REVIEW

18 October, 2013

To Administrative File for STN 125506/0

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Through Dr. William M. McCormick, Director
Division of Biological Standards and Quality Control (DBSQC)

Subject **BLA:** Review of Sterility and Bacterial Endotoxin Test Qualifications and the General Safety Test for Coagulation Factor X (Human).

Recommendation

Based on the scope of this review, I recommend approval of this Biological License Application (BLA)

Conclusion

After a thorough review of this BLA and the response to CBER's Information Request (IR) (amendment 125506/0/7 and 125506/0/11), this reviewer finds the sterility and (b) (4) bacterial endotoxin tests were qualified in accordance with (b) (4) respectively, by showing the Coagulation Factor X (Human) product matrix is suitable for these intended test methods.

Background

Bio Products Laboratory Limited, (b) (4) submitted this BLA on 10 July, 2013 requesting priority review in accordance with Section 506 of the FD&C Act for their product Coagulation Factor X (Human), which from here on will be referred to as FACTOR X.

FACTOR X is a sterile, freeze-dried human coagulation factor X concentrate indicated for haemostatic control in patients deficient in clotting factor X; specifically, to control and prevent bleeding episodes and/or peri-operative management in adults and children (12 years and older) with hereditary factor X deficiency. Bio Products proposes two dose sizes of FACTOR X, that when reconstituted with 2.5 mL or 5 mL water for injection will yield 250 IU or 500 IU per dose, respectively. These two doses will contain the same concentration of active ingredient and chemical formulations, differing only in their corresponding volumes at final container for patient administration.

FACTOR X is derived from human plasma purified to a specific final product activity of (b) (4). FACTOR X is formulated with sodium chloride, citric acid, (b) (4) phosphate sodium chloride, (b) (4) citrate, (b) (4) phosphate and sucrose; but does not contain any preservatives.

The DBSQC reviews BLAs and their Supplements to ensure analytical methods are appropriate, appropriately 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, which is the confirmatory testing of submitted product samples and 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 qualification of the sterility and (b) (4) bacterial endotoxin tests performed on Bio Products' FACTOR X drug product and the bacterial endotoxin test (BET) release specification.

Review

Sterility

Bio Products qualified their FACTOR X product for their compendial (b) (4) sterility test method by performing (b) (4) qualification studies on three batches of FACTOR X (i.e., (b) (4)) to demonstrate if its matrix is suitable for the intended method.

Qualification - (b) (4) Sterility Test

Bio Products qualified their FACTOR X product using (b) (4)



Endotoxin

Bio Products performed their BET using the (b) (4) method on their FACTOR X product matrix in accordance with (b) (4)

Bacterial Endotoxin Test

To qualify the method for their FACTOR X product matrix, Bio Products tested three lots of FACTOR X product (i.e., (b) (4)), as recorded in their analytical method validation report (i.e., QPMV. 1 Ch.6). The maximum valid dilution was calculated to be (b) (4); which is calculated from Bio Products' requested release test specification (i.e., (b) (4))

(b) (4) Bio Products qualified their FACTOR X product matrix for the (b) (4) BET method in accordance with (b) (4) therefore, the FACTOR X product tested at a (b) (4) sample test dilution meets the suitability requirements necessary to qualify its product matrix for the (b) (4) BET method.

The bacterial endotoxin specification is (b) (4) and is based on (b) (4), which is a comparable coagulation factor product to FACTOR X. Therefore, CBER finds Bio Products' final container bacterial endotoxin specification acceptable; however since Bio Products' final container product results in their qualification study are (b) (4), CBER suggests they revise this specification to better reflect their process capability – if necessary – after reviewing the first 30 results or those obtained within two years after the approval of this BLA, whichever comes first.

General Safety

Bio Products' test for general safety (GST) on their FACTOR X product is performed by (b) (4). This facility was inspected by the (b) (4) and certified that it complies with the principles and guidelines in (b) (4). This contract animal testing facility has been performing the GST for Bio Products since approximately (b) (4).

Summary

After a through review of the information submitted in this BLA, this reviewer finds Bio Products' FACTOR X product matrix is suitable for testing using their sterility and bacterial endotoxin testing method; these tests 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.