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DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125833/0

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Applicant Grifols Therapeutics LLC (Grifols)

Subject Review of Bioburden, Endotoxin, and Sterility Analytical Methods for FESILTY® [Fibrinogen (Human) (BT524)]

Recommendation: Approval

Executive Summary:

The bioburden, endotoxin, and sterility analytical methods used for testing and release of FESILTY® and the associated analytic method qualifications or validations, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion:

The analytical methods and their qualifications reviewed for FESILTY® drug substance and drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of Drug Substance (DS) and Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP, and qualifications of these analytical procedures, were reviewed.




Background:

On December 27, 2024, Grifols submitted an original Biologics License Application (BLA) 125833/0 for Fibrinogen (Human) (BT524), with the proposed trade name FESILTY®. FESILTY® is a lyophilized human fibrinogen manufactured from human plasma; it is a human blood coagulation factor indicated for treatment and prophylaxis in patients with congenital hypo- or afibrinogenemia with bleeding tendency.





The drug product is presented as a lyophilized powder for solution for injection / infusion in single-use 100 mL glass vials containing a nominal content of 1 g of lyophilizate. The product is co-packaged as a combination product with 50 mL sterile water for injection (diluent) and a Nextaro® v, 20/20 5 µm transfer device for reconstitution. The active ingredient is purified human fibrinogen concentrate manufactured from the cryoprecipitate fraction of US source plasma, with the biologic constituent serving as the primary mode of action.

This review focuses on the qualification of the bioburden, endotoxin, and sterility tests as performed on the FESILTY® (b) (4) DP, to determine if the product matrix is suitable for testing using the intended test method.

(b) (4)



(b) (4)




2. Bacterial Endotoxin Method (DP)

Introduction

Rabbit pyrogen testing for Fibrinogen Concentrate DP is performed at the contract laboratory, (b) (4) located in (b) (4)

(b) (4) Acceptance criterion of "pyrogen free" must be met for the release of DP.

(b) (4)



Conclusions

The reviewer finds the proposed contract laboratory, (b) (4), performs pyrogen testing in accordance with (b) (4). Therefore, CBER determined their rabbit pyrogen test method is appropriate under the actual conditions of use for the DP.


3. Sterility Method (DP)

Introduction


Sterility testing for Fibrinogen Concentrate DP is performed at Biotest AG in Dreieich, Germany. Specification of 'No Growth Detected' must be met for lot release.

Method

(b) (4)



(b) (4)



Conclusion

The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product inhibition of microorganism growth. Therefore, CBER determined their (b) (4) sterility test method is appropriate under the actual conditions of use.