



CBER REGULATORY REVIEW MEMORANDUM

Date 02 May, 2017

From Simleen Kaur
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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 # 125613/0

Subject BLA: Review of Bioburden, Sterility, Endotoxin and Pyrogen Test Method Qualifications for Human Rabies Immune Globulin

Through James L. Kenney, D.Sc., Chief, LMIVTS/DBSQC/OCBQ/CBER/FDA
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Applicant Kamada Ltd. (Kamada)

Product Human Rabies Immune Globulin (Kamada-HRIG)

Biologics License Application (BLA) Submission Tracking Number (STN) 125613/0

Submission Received by CBER 07 October, 2016

Review Completed 02 May, 2017

Material Reviewed

Method qualifications for: 1) bioburden; 2) sterility; and 3) bacterial endotoxin tests performed on Kamada-HRIG. In addition, procedure for pyrogen test; and information request responses received 02 November and 23 November of 2016 and 04 April and 26 April of 2017 were reviewed.

Executive Summary

After a thorough review of this BLA, this reviewer finds the bioburden, sterility and bacterial endotoxin test methods were qualified in accordance with (b) (4), respectively. In addition, pyrogen test is being performed in accordance with 21 CFR 610.13 (b) and (b) (4).

Background

On 7 October, 2016, Kamada submitted this BLA for Human Rabies Immune Globulin (HRIG) indicated for passive, transient post-exposure prophylaxis of rabies infection, when given immediately after contact with a rabid or possibly rabid animal and in combination with a rabies vaccine.

Kamada-HRIG (b) (4) is manufactured from human hyper immune plasma of healthy donor immunized with rabies vaccine and has developed high titers of rabies antibody. The (b) (4) is tested (b) (4). The drug product (DP) is a sterile, non-pyrogenic liquid preparation with potency of 150 IU/mL and supplied in 2 and 10mL glass vials. The DP is tested for sterility, bacterial endotoxin and pyrogen tests.

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 method qualifications for Kamada’s bioburden, sterility and bacterial endotoxin methods to ensure the product matrix is suitable for these intended test methods and the review of their pyrogen test procedures to ensure they are compliant with the 21 CFR 610.13 (b).

Review

(b) (4)

(b) (4)

(b) (4)

(b) (4)

1 page has been determined to be not releasable: (b)(4)

A second inhibition/enhancement test was performed using (b) (4) [redacted]

After review of (b) (4) method qualification results, this reviewer concludes this method was qualified in accordance with (b) (4) . Kamada submitted the endotoxin results for several (b) (4) DP lots, which met their endotoxin test specification of no more than (b) (4) . CBER finds these proposed specifications acceptable.

Sterility Test Qualification for DP by Kamada and (b) (4)

Kamada has proposed to perform sterility test on HRIG final drug product either in house or by a contracting laboratory, (b) (4) .

The HRIG DP matrix was qualified using the (b) (4) [redacted]

[redacted]

[redacted]

Pyrogen test for Drug Product

The rabbit pyrogen test is a compendial test that does not require suitability qualification testing; however, the test methods (b) (4) : “Rabbit Pyrogen Testing of products For Kamada according to the Current (b) (4)” and N-1P-001-09/2: “(b) (4) Standard Protocol for Pyrogen testing” performed by (b) (4) contracting laboratories, (b) (4) , respectively, were reviewed to ensure they were performed in accordance with 21 CFR 610.13(b) and (b) (4) . In addition, Kamada submitted the rabbit pyrogen test results for several conformance lots of their HRIG DPs and

the results were found to be accordance with 21 CFR 610.13 (b) and (b) (4), indicating an absence of pyrogenic response in their DP matrix.

Conclusion

After a thorough review of the information submitted in this BLA, this reviewer finds Kamada's HRIG matrix is suitable for testing using their bioburden, sterility and endotoxin test methods, as they were qualified and performed in accordance with (b) (4), respectively. In addition, the pyrogen test is being performed in accordance with 21 CFR 610.13(b) and (b) (4). Therefore, this reviewer finds these methods acceptable for their intended purpose and recommends their approval.