



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file: STN 125810/0

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Applicant: Biotest AG

Subject: Review of Bioburden, Sterility, Endotoxin and Analytical Methods used for YIMMUGO (Immune Globulin Intravenous Human, 10% Liquid, IgG Next Generation [BT595]) and appropriateness of CBER Standard use for U.S. Diphtheria Antitoxin for Neutralization.

Recommendation: Approval.

Executive Summary:

The bioburden, sterility, endotoxin, and diphtheria antitoxin potency analytical methods used for testing and release of YIMMUGO (Immune Globulin Intravenous Human, 10% Liquid, IgG Next Generation [BT595]) and the associated analytic method qualifications, 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 YIMMUGO (Immune Globulin Intravenous Human, 10% Liquid, IgG Next Generation [BT595]) (b) (4) (b) (4) drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe control of (b) (4) (b) (4) Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of (b) (4) DP specifications, analytical procedures of (b) (4) DP and qualifications of these analytical procedures were reviewed. In addition, the responses to CBER's Information Requests (IRs) received on October 12, 2023 (Amendment # 18) and January 19, 2024 (Amendment #45), were also reviewed.

1. Bioburden Test on (b) (4)

Introduction

This test is performed on (b) (4) by Biotest AG in Dreieich, Germany. Specification of (b) (4) (b) (4) must be met for both (b) (4) and (b) (4) (b) (4) for lot release of YIMMUGO (b) (4)

Review of Method:

(b) (4)

(b) (4)

Conclusion

The method suitability test was performed and compliant with (b) (4) thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use.

2. Endotoxin test on (b) (4)

Introduction

This test is performed on (b) (4) Biotest AG in Dreieich, Germany. Specification of (b) (4) (b) (4) must be met for lot release of YIMMUGO (b) (4)

Review of Method:

(b) (4)

(b) (4) The method is described in more detail below together with the tests that were performed to demonstrate suitability of the test method for its intended use.

Review of Method Qualification:

Biotest AG qualified their (b) (4)

(b) (4)

(b) (4)

Conclusion:

Biotest AG submitted bacterial endotoxin concentration results from (b) (4) lots, and all were within their release specification (b) (4). The method suitability tests were performed and compliant with (b) (4) thus indicating the (b) (4) test method is appropriate under the actual conditions of use.

3. Sterility Test on DP

Introduction

This test is performed on DP by Biotest AG in Dreieich, Germany. Specification of 'No Growth Detected' must be met for the lot release of YIMMUGO DP.

Review of Method

(b) (4)

The method is described in more detail below together with the tests that were performed to determine suitability of the test method for its intended use.

Review of Method Qualification:

Biotest AG qualified their (b) (4) method at their Dreieich, Germany facility using their YIMMUGO DP by performing (b) (4) qualification studies to determine if the method is suitable under the actual conditions of use. The tests were performed using (b) (4)

(b) (4)

(b) (4)

(b) (4)

Conclusion:

The method suitability test was performed and compliant with (b) (4) thus indicating the (b) (4) test method is appropriate under the actual conditions of use.

4. Endotoxin test on DP

Introduction

This test is performed on DP by Biotest AG in Dreieich, Germany. Specification of (b) (4) must be met for lot release of YIMMUGO (b) (4)

Review of Method:

(b) (4)

The method is described in more detail below together with the tests that were performed to demonstrate suitability of the test method for its intended use.

Review of Method Qualification:

Biotest AG qualified their (b) (4) method for their DP, to demonstrate the method is suitable under the actual conditions of use in accordance with (b) (4). The (b) (4) test was qualified by testing (b) (4) lots of (b) (4) of DP. (b) (4)

(b) (4)

(b) (4)

(b) (4)

CBER finds acceptable.

Conclusion:

Biotest AG submitted bacterial endotoxin concentration results from DP lots, and all were within their release specification (b) (4). The method suitability tests were performed and compliant with (b) (4) thus indicating the (b) (4) test method is appropriate under the actual conditions of use.

5. Diphtheria Toxin Neutralization Potency Tests – Documentation of correspondence regarding the appropriateness of CBER Standard Use

The Product Office is reviewing the Diphtheria Toxin Neutralization potency tests. However, as CBER produces and distributes the U.S. Standard Diphtheria Antitoxin, we communicated with the PO about our concerns regarding Biotest AG's use of CBER's U.S. Standard Diphtheria Antitoxin, as outlined below.

(b) (4)

(b) (4)

Regardless of the above-mentioned concerns, CBER is committed to advancement in scientific alternate methods that reduce, refine, or replace the use of animals.

Furthermore, while the standard has not been qualified for use in either the (b) (4) (b) (4) tests, the standard does provide a way to determine relative quantity of (b) (4) present in the sample using (b) (4) assays.