

DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: BLA STN 125810/0

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Product: YIMMUGO (Intravenous 10% human Immune globulin, IgG Next Generation (BT595))

Applicant: Biotest AG

Subject: Review of Analytical Methods used for YIMMUGO (Intravenous 10% human immune globulin (b) (4) Drug Product (DP) and Lot Release

Recommendation: Approval

Summary:

The following analytical methods used for lot release of YIMMUGO and the associated analytical method validations were reviewed:

1. Determination of antibodies against Hepatitis B surface antigen (HBsAg) by (b) (4)
2. Determination of immunoglobulin content by (b) (4)
3. Determination of the composition of immunoglobulins (IgG, IgA, IgM) by (b) (4)
4. Identification of (b) (4)
(b) (4)
5. Determination of (b) (4)
(b) (4) hemolysis
6. Determination of (b) (4) assay

Conclusion:

The analytical methods and their validations reviewed for the YIMMUGO (b) (4) (b) (4) drug product (DP) were found to be adequate for their intended use.

Documents Reviewed:

Information in sections of the original submission that describe control of (b) (4) 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 validation of these analytical procedures were reviewed. Additional information received on December 21, 2023, in the Amendment 125810/0.36 was also reviewed.

Background:

On June 30, 2023, Biotest submitted an original BLA, STN 125810/0, for YIMMUGO (IgG Next Generation (BT595)), a new intravenous human immunoglobulin (IVIG) for the treatment of primary humoral immunodeficiency (PI) in patients 2 years of age or older. The active ingredient of YIMMUGO is human immunoglobulin G (IgG) purified from source human plasma and contains 100±10 mg/mL protein, with at least 96% IgG and a maximum of (b) (4) IgA and (b) (4) IgM. YIMMUGO is manufactured at the Biotest AG manufacturing site in Dreieich, Germany and supplied in 5g/50mL, 10g/100 mL, and 20g/200 mL single-dose vials.

Review:**1. Determination of antibodies against Hepatitis B surface antigen (HBsAg) by ELISA**Introduction

The test for antibodies against Hepatitis B surface antigen (HBsAg) is performed based on (b) (4) (b) (4) is used to determine the antibodies against HBsAg in YIMMUGO (b) (4) DP for release and stability testing.

Method

(b) (4)

(b) (4)

Method Validation

(b) (4)

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(b) (4)

Conclusion

The method for determination of antibody to HBs antigen with the (b) (4) assay was well described and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.

Comparison of (b) (4)

(b) (4)

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(b) (4)

2. Determination of immunoglobulin content by (b) (4)

Introduction

The immunoglobulin content is determined by (b) (4) according to the (b) (4) and (b) (4) (b) (4) YIMMUGO (b) (4) DP.

Method

(b) (4)

Method Validation

(b) (4)

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(b) (4)

Conclusion

Determination of immunoglobulin content by (b) (4) was well described and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.

3. Determination of the composition of immunoglobulins (IgG, IgA, IgM) by (b) (4)

(b) (4)

Introduction

The composition of the immunoglobulins of IgG, IgA and IgM is determined by (b) (4) (b) (4) method according to the (b) (4)

Method

(b) (4)

Method Validation

(b) (4)

3 pages have been determined to be not releasable: (b)(4)

(b) (4)

Conclusion

Determination of IgG, IgA, IgM by (b) (4) was well described, and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.

4. Identification of (b) (4) (b) (4)

Introduction

The identity and (b) (4) is examined by (b) (4)
(b) (4) according to (b) (4) on (b) (4) according to (b) (4)
(b) (4)

Method

(b) (4)

Method Validation

(b) (4)

(b) (4)

Conclusion

Identification of (b) (4) was well described and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.

5. Determination of (b) (4) hemolysis

Introduction

The (b) (4) is determined according to the (b) (4)
2.6.17 (Test for (b) (4))

Method

(b) (4)

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(b) (4)

Conclusion

The method for the determination of (b) (4) DP was well described and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.

6. Determination of (b) (4) assay

Introduction

The (b) (4) test for (b) (4) is performed according to (b) (4)
(b) (4)

Method

(b) (4)

Method Validation

(b) (4)

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(b) (4)

Conclusion

(b) (4) assay for the determination of (b) (4) was well described and the validation test results complied with the predefined acceptance criteria. Therefore, the method is appropriately validated and is suitable for its intended use.