



MEMORANDUM

From: Hsiaoling Wang, Ph.D.
CMC Reviewer
Laboratory of Analytical Chemistry and Blood Related Products (LACBRP)
Division of Biological Standards and Quality Control (DBSQC)
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 125683/0

Subject: Review Memo for Immune Globulin Subcutaneous (Human) 20%, XEMBIFY®

Through: Lokesh Bhattacharyya, Ph.D., Lab Chief, LACBRP/DBSQC/OCBQ/CBER

Maryna Eichelberger, Ph.D., Director, DBSQC/OCBQ/CBER

Applicant: Grifols Therapeutics LLC.

Submission Received by CBER: July 09, 2018

Summary:

A new BLA (STN 125683/0) was submitted by Grifols for Immune Globulin Subcutaneous (Human) 20% product for the treatment of primary immunodeficiency in adults and children.

This document constitutes the Review Memo from DBSQC for the analytical method and the validation of (b) (4)

which is proposed to be used for lot release of the drug product (DP).

This reviewer found that the analytical procedure is adequately described and validated for its intended use.

Background

XEMBIFY is a formulation of human normal immunoglobulin (IgG, 20%) prepared from human plasma. It is supplied in 5 mL, 10 mL, 20 mL and 50 mL (b) (4) glass vials for subcutaneous administration.

Documents Reviewed

Original submission STN 125683/0 dated July 9, 2018

- Cover letter
- 2.2 Introduction
- 2.3 Quality Overall Summary
- 3.2.S.4.1 Specification
- 3.2.S.4.2 Analytical procedure
- 3.2.S.4.3 Validation of Analytical Procedure
- 3.2.S.4.4 Batch analysis
- 3.2.S.5 Reference Standards or Materials
- 3.2.P.1 Description and composition of the Drug Product
- 3.2.P.5.1 Specification(s)
- 3.2.P.5.2/3.2.P.5.3 Analytical Procedures and Validations
- 3.2.P.5.4 Batch analysis
- 3.2.P.5.5 Characterization of Impurities
- 3.2.P.6 Reference Standards or Materials
- Standard Operating Procedure (Doc# CS-000-BC-034): (b) (4)
- Validation Report (Doc# QOAS-2014-116): Validation of (b) (4)

IGSC

Amendment 15, dated December 14, 2018

- 1.12.11 Basis Statement – Response to IR #10

Amendment 24, dated February 28, 2019

- 1.12.11 Information Request #17 Response

Amendment 31, dated April 5, 2019

- 1.12.11 Information Request #22 Response

Amendment 32, dated April 30, 2019

- 1.12.11 Information Request #25 Response

Amendment 39, dated June 5, 2019

- 1.12.11 Information Request #30 Response

2 Pages have been determined to be not releasable: (b)(4)

(b) (4)

Information Request (IR) and Review of Response

The following IRs were sent to sponsor on Nov. 21, 2018 because deficiencies found in accuracy, linearity, range and robustness evaluation of the (b) (4) and linearity and LOQ evaluation of (b) (4) in the validation report. The responses were received on Dec. 14, 2018 in the Amendment 15.


- a. In the appendix C of the SOP, it is stated that samples must be capable (b) (4) How would this procedure apply to the drug product of Immune Globulin Subcutaneous (Human), 20%?

Review of the response: The sponsor clarified that DP samples are (b) (4) in the response. The response is satisfactory.

- b. Method validation report (DOC#: QOAS-2014-116).


(b) (4)

(b) (4)


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The second IR were sent to the sponsor on Feb. 14, 2019 and the response was received on Feb. 28, 2019 in Amendment 24.


(b) (4)

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(b) (4)




(b) (4)




The third IR were sent to the sponsor on March 22, 2019 and the response was received on April 5, 2019 in Amendment 31.

(b) (4)

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The fourth IR are sent to the sponsor on April 17, 2019 and the response was received on April 30, 2019 in Amendment 32.

(b) (4)

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(b) (4)

A follow-up IR was sent.

The fifth IR were sent to the sponsor on May 29, 2019 and a tele-conference was held on June 4, 2019. This reviewer provided an example of data normalization when (b) (4). The scientists from Grifols were happy with the solution FDA provided and the response was received on June 5, 2019 in Amendment 39.

(b) (4)

(b) (4)

Conclusion: (b) (4) assay is adequately described and validated for the intended use.