

From: Maruna, Thomas
Sent: Wednesday, January 20, 2016 3:01 PM
To: 'Denloye, Aderonke O'
Subject: January 20. 2016 Information Request - BLA 125596.0 - Please Respond by February 3. 2016

Importance: High

Baxalta US Inc.
Attention: Ms. Aderonke Denloye
January 20, 2016
Sent by email

Dear Ms. Denloye:

We are reviewing your September 14, 2015 biologics license application (BLA) to treat primary immune deficiency disorders associated with defects in humoral immunity for the following:

STN	Name of Biological Products
125596/0	Immune Globulin Subcutaneous (Human), 20% Solution

We have determined the following information is required to continue our review:

We have reviewed the quality control test methods for the drug product (STN: 125596) and the respective validation reports. We have following information requests for the indicated assays.

1. (b) (4)
The method is still under re-validation upon FDA request (dated Nov. 30, 2015).
 - a. However, the precision evaluation for the method was submitted PV-LA-09.007 in amendment 01 (dated Oct. 14, 2015). Three out of (b) (4) results (Table 5) failed to meet the set acceptance criteria. Please explain why the precision study can be considered satisfactory.
 - b. For the submitted re-validation procedure dated Dec. 11, 2015. We don't agree with your accuracy study proposal. (b) (4) requirement doesn't address the accuracy but the specificity. The accuracy of this assay can be determined by performing spike-recovery study with a (b) (4) IgG sample.

2. **Octoxynol 9** by (b) (4)
 - a. In the validation report (PV-LA-14.012), the calculated LOQ is (b) (4) . However, for the intermediate precision study at spiking level of (b) (4) . Thus the LOQ at (b) (4) is not acceptable. Please reevaluate the LOQ value based on the outcome of linearity, accuracy and precision.
 - b. A calibration curve with the lowest octoxynol 9 standard concentration at LOQ or above is meaningful. Please make revision in your Control Test Procedure (CTP) or SOP.

- c. Please note that the test results that are below LOQ should be expressed as < LOQ. The results of (b) (4) reported in the batch analyses (3.2.P.5.4) should be reported as < LOQ (b) (4).

3. Purity by (b) (4)

- a. Please include a typical (b) (4) of IGSC 20% DP sample in the CTP.
- b. Please provide sample preparation details, including dilution factor or protein concentration for IGSC 20% DP samples (b) (4) in the CTP. Also, please revise your CTP to include (b) (4) conditions such as (b) (4) and resubmit for review.

4. Total Protein By (b) (4)

As evaluated in the validation report (PV-LA06.022), the LOQ of the assay is (b) (4). However, the (b) (4) from (b) (4) IGSC 20% sample has a typical (b) (4) value of (b) (4) (page 4 of LE-65-A25002S), which is below the LOQ. Please revise the CTP (LE-13-A26002-CTP00) to (b) (4) the sample volume for the determination of (b) (4) of IGSC 20% DP to make sure that the (b) (4) value is above LOQ to obtain appropriate value of (b) (4) for calculation of (b) (4) in the sample.

5. Glycine by (b) (4)

In the specificity section of the validation report (LE-65-A25002S), you stated that the (b) (4). Please provide scientific literature reference(s) for this conclusion.

Please submit your responses to question 1 as an amendment to this file by February 3, 2016 referencing the date of this request.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

The action due date for these files is September 13, 2016.

If you have any questions, please contact me.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP)^{CM}

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