

From: Do, Yu
Sent: Friday, January 08, 2016 3:31 PM
To: dmyers@malvernconsultinggroup.com
Subject: Information Request (Response Due by Friday, January 29, 2016): Original BLA, BL 125590/0, Immune Globulin Intravenous (RI-002), ADMA Biologics, Inc.

Importance: High

Dear Ms. Myers:

We are reviewing your original July 31, 2015 submission to BLA 125590/0 for Immune Globulin Intravenous (Human). We are providing the following comments and request additional information to continue our review:

1. In various sections of the BLA pertaining to the (b) (4) assay, you listed three different reference standards for calibration or qualification purposes (e.g., (b) (4) Reference Standard, (b) (4) reference material (b) (4), and (b) (4) standard).

Please clarify which reference standard will be the sole basis for calculating the (b) (4) of the final drug product. In addition, for the chosen reference standard, please provide the following supporting information:

- a. A detailed description of the reference standard, including its source, reported (b) (4), preparation, and storage conditions
- b. Qualification study report for the use of the reference standard
- c. Stability data

2. To prevent further confusion, we suggest that you revise the wording of your (b) (4) Drug Product Specification to indicate which reference standard you will be using as the basis for calculating the (b) (4) (i.e., not the internal standard).

3. With regard to Questions 1 and 2, please revise the appropriate sections of the BLA accordingly to clarify which reference standard you will use to calculate the (b) (4)

4. In order to ensure that the formulation of your final product does not affect the (b) (4) assay results, please perform additional (b) (4) testing of the final product using (b) (4) methods and compare the outcomes, if possible. You may use assays that are commercially available, e.g., a (b) (4) assay.

5. Please provide the method validation report from (b) (4) regarding their Polio neutralization assay.

6. Endotoxin test: Two SOPs, QC2147 and QC3121, are listed under 2.3.R Regional Information and 3.2.R Regional Information. Only QC2147 is listed under 2.3.S Control of (b) (4), 3.2.S.4.1 Specification, 2.3.P Control of Drug Product, and 3.2.P.5.1 Specifications.

- a. Please indicate which SOP was used in your process validation.

- b. Please clarify which SOP corresponds to the validation report VP-FR-3558.
- c. What is the difference between QC2147 and QC3121?

7. (b) (4) test: Two SOPs, QC3192 and QC2194, are listed under 2.3.R Regional Information and 3.2.R Regional Information. Only QC3192 is listed under 2.3.S Control of (b) (4), 3.2.S.4.1 Specification, 2.3.P Control of Drug Product, and 3.2.P.5.1 Specifications.

- a. Please indicate which SOP was used in your process validation.
- b. Do you intend to use both SOPs for your (b) (4) Drug Product lot testing? If yes, please indicate which SOP will be the primary method.

8. (b) (4) test: Two SOPs, QC3178 and T:EA-148-02, are listed under 2.3.R Regional Information and 3.2.R Regional Information. Only QC3178 is listed under 2.3.S Control of (b) (4) and 3.2.S.4.1 Specification.

- a. Please indicate which SOP was used in your process validation.
- b. Do you intend to use both SOPs for your (b) (4) lot testing? If yes, please indicate which SOP will be the primary method.

9. (b) (4) test: Two SOPs, QC3117 and T:EA-139-02, are listed under 2.3.R Regional Information and 3.2.R Regional Information. Only QC3117 is listed under 2.3.S Control of (b) (4) and 3.2.S.4.1 Specification.

- a. Please indicate which SOP was used in your process validation.
- b. Do you intend to use both SOPs for your (b) (4) lot testing? If yes, please indicate which SOP will be the primary method.

The review of this submission is ongoing and issues may be added, expanded upon, or modified as we continue to review this submission. Please submit your response as an amendment to this file by January 29, 2016, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is July 30, 2016.

Please acknowledge receipt of this request and contact me at (240) 402-8343 or Yu.Do@fda.hhs.gov if you have any questions.

Sincerely,

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