

From: Wittig, Anja <anja.wittig@octapharma.com>  
Sent: Wednesday, 02 May, 2018 04.41  
To: Levi, Mark  
Cc: Rangetiner, Barbara  
Subject: RE: FDA IR for BLA 125587

Sensitivity: Confidential

Dear Mr. Levi,  
I confirm receipt of your email.  
Kind regards,  
Rita Gorsche

On behalf of  
Anja Wittig  
Manager  
International Regulatory Affairs Department

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From: Rangetiner, Barbara  
Sent: Dienstag, 01. Mai 2018 17:24  
To: Wittig, Anja; Gorsche, Rita  
Cc: Rangetiner, Barbara  
Subject: FW: FDA IR for BLA 125587  
Sensitivity: Confidential

From: Levi, Mark [mailto:Mark.Levi@fda.hhs.gov]  
Sent: Dienstag, 01. Mai 2018 14:57  
To: Rangetiner, Barbara <barbara.rangetiner@octapharma.com>  
Cc: Ammons, Stanley <stanley.ammons@octapharma.com>  
Subject: FDA IR for BLA 125587  
Sensitivity: Confidential

Our Reference: BL 125587/0

Dear Dr. Rangetiner:

We are reviewing your resubmitted biologics license application for Immune Globulin Intravenous (Human) 10. We determined that the following information is necessary to continue our review:

1. Please explain the increase in (b) (4) results in the current PPQ batches (report 020STD82x.433/00) compared to the consistency batches manufacture in 2014 (report 020STD821.826.278/00).
2. Please provide a list of Process segments and time limits (ranges)
3. Please provide a table of Step (b) (4) pH readjustment for all the conformance lots and the corresponding impurities measured after this step. Please explain how the (b) (4) amount was determined and why the pH has to be readjusted after this addition.
4. Please provide a table of the manufacturing and expiration dates for all the conformance batches.
5. For the maximum process conditions under which the conformance batches were produced, did you also challenge the maximum mixing speeds? If so, please provide the list of mixing speeds used at each step.
6. Please explain the acceptance criterion and results for final container (b) (4) Table 45 in report 150PPQR1726/00. Your Drug Product specification for (b) (4); however, your acceptance criteria ((b) (4)) and results ((b) (4)) are above the Drug Product specification and stability specification ((b) (4)) and results ((b) (4)) in report 17P012.
7. Please justify the specifications for (b) (4), Sodium, (b) (4), and IgA based on PPQ and historical lot results to date.
8. Please provide an update on your ongoing stability studies. Please also update your stability tables to include the proposed revision of the limit for “Fragments”, i.e., “Fragments (b) (4)”.  
(b) (4)
9. In your response to Question 15b, it stated that the in-process acceptance criteria for (b) (4) concentration of sample (b) (4) and sample (b) (4) were calculated based on “(b) (4)”, however in the corresponding supporting document 150PPQR1726/00 (tables 48 and table 50), it appeared that they had been calculated based on “(b) (4)” instead. In addition, it is unclear how the obtained values were then used to set the “setting limit min” and “setting limit max”. Please explain, and also provide the (b) (4) test results for the (b) (4) additional manufacturing batches, which had been used in rechecking the preliminary limit for (b) (4) content, in the (b) (4).
10. In the (b) (4) validation study, “Influence of Storage Temperature at ? (b) (4) were studied using batch (b) (4). The test results for (b) (4) samples showed as “trend observed ?failed” on both page 97 and page 104, however in the corresponding discussion sections you concluded that “there was no trend observed according to (b) (4) test. Therefore, (b) (4) Panzyga (b) (4) samples can be stored for (b) (4)”. Please clarify these apparent discrepancies.
11. In the file 150ADD1726/00 – Addendum to Process Validation Report – 2017, it stated that both lot (b) (4) will not be marketed in USA (pages 9 and 10). Please indicate if they are manufactured for non-US market originally or subjected to re-allocation. Please provide a copy of SOP that is used for allocation and/or re-allocation of manufactured batches in OSA.

12. Please provide a list of the filters and how many are used per batch. Please provide information on how many of each filter are used per batch, how are they configured (parallel, sequential), and whether they are changed out. Please state how many filters were used in each step during the manufacture of the conformance lots.

13. Please correct the IgG content on the label from (b) (4) .

14. Please provide the executed batch record of the maximum process time lot.

15. Please provide the (b) (4) content test results for Samples (b) (4) and final container from the (b) (4) Panzyga lots manufactured (b) (4) .

16. Please provide the Extractables and Leachables (E/L) studies and risk assessment conducted for using (b) (4) step. Please provide a copy of material specification for the (b) (4) , and a copy of SOP for (b) (4) .

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

Please submit your response to this information request as an amendment to this file by May 15, 2018, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact me 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.

Please confirm receipt of this email.

The action due date for this file is Sept. 28, 2018.

Regards, Mark Levi  
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Regulatory Project Management Staff  
Center for Biologics Evaluation and Research  
Office of Tissues and Advanced Therapies  
U.S. Food and Drug Administration  
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