

From: Hooban, Christopher
Sent: Monday, November 30, 2015 10:36 AM
To: Krammer, Marlene
Cc: Rangetiner, Barbara; Ammons, Stanley; Cagungun, Nannette
Subject: RE: BL 125587/0 - Information Request (25 NOV)

Ms. Krammer,

Good morning. You are correct. The document (753RVP009/00) is only needed once. Also, the reviewer is ok with a response date of 11 DEC but would like to request that any information that is collected prior to 4 DEC be submitted on 4 DEC with the remainder being submitted by 11 DEC. Thanks for your time.

Chris

From: Krammer, Marlene [mailto:marlene.krammer@octapharma.com]
Sent: Monday, November 30, 2015 5:24 AM
To: Hooban, Christopher
Cc: Rangetiner, Barbara; Ammons, Stanley; Cagungun, Nannette
Subject: RE: BL 125587/0 - Information Request (25 NOV)

Dear Chris,

I refer to your Email dated November 25, 2015 in regards to BL 125587/0. Could you please clarify the following? Document 753RVP009/00 is requested twice, in question Q3c and Q3d. Could you please confirm that this document is only needed once?

In addition we kindly ask FDA to extend the deadline for submitting the responses to December 11, 2015. Could you please let us know if the proposed new deadline is acceptable for FDA?

Kind regards, Marlene

Marlene Krammer
Manager
International Regulatory Affairs Department

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From: Hooban, Christopher [mailto:Christopher.Hooban@fda.hhs.gov]
Sent: Wednesday, November 25, 2015 11:42 AM
To: Ammons, Stanley
Cc: Cagungun, Nannette

Subject: BL 125587/0 - Information Request (25 NOV)

Our Reference: BL 125587/0

Dear Mr. Ammons:

We are reviewing your April 15, 2015 biologics license application (BLA) for Immune Globulin Intravenous (Human), 10%. We are providing the following comments and request for additional information:

1. In your stability studies, the result for parameter of Clarity ((b) (4)) was shown as either “according” or “not demanded”. Please confirm if these meant “pass” or “not determined.”
2. The mixing duration range after (b) (4) in your process validation and/or evaluation report (3.2.S.2.5) as well as in mixing study (753RVP007/00). However, in your batch record, the maximum stirring time of (b) (4) is not indicated. Please correct it and add the maximum stirring time to your Master Batch Record (MBR).
3. In your mixing study report (753RVP009/02), the validated stirring speed range is set as the range of (b) (4), which is different from the one shown in your MBR ((b) (4)). Please clarify this discrepancy and indicate if the range of (b) (4) has been validated. Please provide your supporting document(s) which show(s) how the stirring speed range of (b) (4) was initially determined. Please provide the following documents for agency’s review:
 - a. Mixing study protocol ((b) (4)) 753PVP009/02
 - b. 753RVP009/01
 - c. 753RVP009/00
 - d. 753RVP009/00
 - e. 753RVP004/01
 - f. 753RVP004/00
4. Please provide the batch record of (b) (4) from Step (b) (4) to Step (b) (4) Nanofiltration.
5. In your deviation 37097, as part of the CAPA, the procedure 753MOS016 was updated to enable (b) (4) is not acceptable, and it is recommended to keep your previous version of 753MOS016 unchanged and modify Master Batch Record accordingly. Please provide a copy of the final 753MOS016 and MBR for review after modifications. Please commit not to releasing the lots (b) (4) lots made from lot (b) (4) associated with deviation 37097, to the US market.
6. The investigation report for your deviation 25282 indicated that “according to the process experts on the Vienna site, the disruptions to the (b) (4) stage could be the cause of the (b) (4) nanofiltration stage”. Please provide the justification or evidence for this explanation.
7. For deviation 37429, the root causes were not clearly identified but it stated that it could be a combination of several factors let to (b) (4)

(b) (4)

8. For the (b) (4) steps, please provide the information on how the (b) (4)-runs in production scale was determined as the lifetime of the (b) (4) .

9. Regarding the (b) (4)

10. Please change the Measles Ab specification in the lot release protocol to (b) (4) NIH 176 as agreed to during the PAI.

11. Please provide the short supply agreement for the (b) (4) plasma, which should include: collection, (b) (4), storage, and shipment conditions for (b) (4) plasma for further manufacture into IGIV.

12. Please provide an update on CAPAs 24404 and 25342. Please provide a list of any deviations which have occurred since the implementation of these CAPAs that are related to the same root cause(s).

13. In Deviation 36930, the (b) (4) was out of the (b) (4) range. You mention that you will update the range to (b) (4) due to the range being set incorrectly after (b) (4) technical runs. Please provide a justification on why the range will be changed after only one lot is out-of-range. The process validation should confirm already determined parameters.

14. Following the review of the October 19, 2015 IR response, it is still unclear if all the issues that were encountered during the conformance batch manufacturing were resolved. Please provide a list of the manufacturing changes between the conformance lots and the consistency lots.

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 December 4, 2015 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.

The action due date for this file is April 14, 2016.

If you have any questions, please contact Christopher Hooban at (240) 402-8376 or christopher.hooban@fda.hhs.gov.

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