

From: Hooban, Christopher
Sent: Thursday, August 27, 2015 10:53 AM
To: Ammons, Stanley
Cc: Cagungun, Nannette
Subject: Information Request - STN 125587/0

Our Reference: BL 125587/0
Original BLA

Octapharma Pharmazeutika Produktionsges.m.b.H.

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 to continue our review:

1. Please confirm that you use dedicated (b) (4) ion-exchange columns for lots manufactured for the US market.
2. Please provide the proposed validation study of sample storage time with (b) (4) if it has been performed. If not, please indicate when this study report will be available for review.
3. Please provide a complete list of deviations occurred during the process validation, along with the corresponding investigation reports.
4. For the STEP (b) (4) Nanofiltration, what is the process (b) (4) for the step of “the product (b) (4)”? Was the same (b) (4) step performed in the conformance lots manufactured in 2013?
5. Please provide detailed information on the issues/deviations that were encountered during the conformance batch manufacturing, i.e., (b) (4) during nanofiltration. Please provide detailed information on how these issues/deviations were fixed.
6. Please provide the reference documents [12] and [13] indicated in page 64/93 of the Comparability Study Report:
“Additional studies were performed following the issues during production of the conformance batches 2013 to investigate the impact of (b) (4) during nanofiltration step. Both conditions investigated did not impact the viral safety of the product.”
[12] 2/14/03/751/4/07: Impact of (b) (4) on PPV removal on (b) (4) 20N NF
[13] 2/14/04/751/4/11: Impact of (b) (4) on PPV removal on (b) (4) 20N NF
7. Please explain how the acceptance criteria of process control parameters for each processing steps were established.
8. In the Comparability Study Report, please clarify how the pilot scale batches were chosen. Please refer to the following Tables listed in the report: Table 8, Table 11, Table 12, Table 13, Table 16, Table 18, Table 19 and Table 20. Please provide the raw

data in an excel spreadsheet for individual lot being used in the comparability study report.

9. At step (b) (4)

if not, please explain how the final concentration of (b) (4) is achieved accurately.

10. Please provide a complete list of the technical batches used in the mixing studies, along with the following information (if applicable): batch numbers, filling sizes, production scales, manufacture sites, and manufacture dates.

11. Please provide the validation reports for the following step/testing:

- a) The integrity tests for the (b) (4) filter (b) (4) use at Nanofiltration step
- b) The integrity tests for the (b) (4) filter (b) (4) use in the bulk filtration.

12. For a mixing study, the worst case scenarios should include both the minimum and maximum batches to ensure that (b) (4) at minimum batch size and (b) (4) at maximum batch size can be assessed. However only the maximum (b) (4) was considered in all the mixing studies except the one for (b) (4). Please provide your justification why the minimum batch sizes were excluded in your studies and why no worst case scenarios were considered in the mixing study for (b) (4). Please provide your estimate of how the worst case conditions may impact the product stability. Please also indicate which lots under the stability studies were manufactured under the worst case conditions. Please provide your justification if no such lots have been included.

13. Please provide the life cycle validation reports for the units of (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 September 28, 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 me at (240) 402-8376 or christopher.hooban@fda.hhs.gov.

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