

From: Hooban, Christopher
Sent: Tuesday, June 23, 2015 8:25 AM
To: Ammons, Stanley
Cc: Cagungun, Nannette
Subject: Information Request BL 125587/0; Original BLA; Octapharma; ADD 14-APR-2016

Our Reference: BL 125587/0

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 determined that the following information is necessary to continue our review:

As a follow-up to our discussion on June 10, 2015 regarding the filling operations of NewGam at the OPG Vienna facility (BLA 125587 for Immune Globulin Intravenous Human, 10%), we request that you respond to all the issues discussed during the telecon with specific attention to the items listed below. The information requested is necessary to continue our review and evaluation of the filling operations of NewGam at OPG.

In your response to these questions please describe the deviations/non-conformities that were raised, and how they were resolved.

Cleaning and Sterilization/sanitization

1. In the BLA submission you presented a summary report of the cleaning validation of the equipment and the acceptance criteria. As we discussed during the June 10 telecon, it was not clear whether (b) (4) sampling was performed and what were the acceptance criteria. Moreover, please describe the (b) (4) sampling and justify the acceptance criteria.
2. Please provide in a Table format the equipment used for Line-(b) (4) and Line-(b) (4) filling (and both lines), the cleaning process ((b) (4), washing machine, manual), and sampling performed ((b) (4)). Also include the sanitization/sterilization process used ((b) (4), autoclave) for the relevant equipment.
3. In the BLA submission you listed (b) (4) autoclaves used for the sterilization/sanitization associated with Filling Line (b) (4) and Filling Line-(b) (4). Please provide a description of the autoclaves, and list the different validated loads and the cycle parameters for the different sterilization/sanitization cycles associated with NewGam production. Clarify if the qualification of the autoclaves and the validation of the sanitization/sterilization of the different loads used in NewGam production has been submitted, reviewed and approved in association with other licensed products (provide STN and approval date). Please state the revalidation program for the autoclaves and provide the latest revalidation report for both autoclaves.
4. You stated that (b) (4) sterilizers (b) (4) are used for stoppers and caps. Please describe the sterilizers, provide the qualification including empty chamber mapping, and the validation of the different loads associated with Line-(b) (4) (300mL presentation) and Line-(b) (4) (both presentations). Please describe the loads and clarify whether they are defined, or variable.
5. Please list the validated dirty, clean and sterile hold times for the equipment associated with the production of NewGam, and provide supportive data.

Container Closure:

6. There are several vial presentations and stoppers used for the filling of NewGam. As we

discussed during the June 10 telecon, there were inconsistencies whether the stoppers were cleaned /sterilized or just sterilized and whether the bottles were (b) (4) or not. Please provide in a Table format the vials used ((b) (4)) or not and whether that is performed in house), and stoppers (cleaned, sterilized – in house or by the supplier).

7. You clarified during the June 10 telecon that container closure integrity was tested using the (b) (4) method on several lots filled at OPG and OSA during the stability studies. Please describe the CCIT method used, the number of vials/bottles used and how it was validated (include conditions of testing and positive and negative controls), and provide the results.

Filling Line-(b) (4)

8. Line-(b) (4) has been approved for the filling of Albumin and Octagam. You stated during the June 10 telecon that the containers/closures used for NewGam are the same as those used for the licensed products with the exception of the 300mL vials – only used for NewGam. Please provide the validation of the vial washing cycle, depyrogenation, filling, stoppering, and capping for the new 300mL presentation.

Filling Line-(b) (4)

9. You confirmed during the June 10 telecon that Line-(b) (4) ((b) (4)) product contact equipment: tubing and needles) is not licensed for filling US products; and you added that it is used for filling non-US products. You stated that filling/stoppering is performed using (b) (4) technology (Grade (b) (4)) and capping is performed using (b) (4) under Grade (b) (4) air supply. You also stated that the qualification, cleaning and sterilization of stainless steel vessels used to support filling on Line-(b) (4) have not been reviewed/approved by FDA.

10. Please provide the protocols and summary report(s) for the validation of cleaning and sterilization of the vessels and state how that compares to routine operations.

11. As we discussed during the telecon, the following information is necessary for us to review and evaluate the new filling Line-(b) (4):

a. Schematic diagram of the filling/stoppering/capping within the (b) (4) with the locations of the (b) (4)

b. Qualification of the equipment and validation of the processes (cleaning, sterilization/sanitization, depyrogenation, (b) (4), etc...), associated with Filling Line-(b) (4):

i. Vial washer, depyrogenation tunnel, filling/stoppering/capping, (b) (4), and tanks. Please provide protocols and summary reports.

ii. For the cleaning and (b) (4) of the (b) (4), please provide validation of the (b) (4) cycle and (b) (4) cycle. Please include schematic diagram/photos showing the locations of the BIs (biological indicators) in the loaded (b) (4) during the validation cycle, and why these are considered worst case.

1. Are the (b) (4) placed (b) (4) prior to (b) (4)? Please clarify whether (b) (4) testing is performed on (b) (4) after the (b) (4) and provide results of the studies performed.

c. Please describe the studies performed and the summary reports for the classification of the (b) (4) and background area under static and dynamic conditions. Please describe EMPQ (environmental monitoring performance qualification) to support the filling of NewGam using Line-(b) (4), and provide the summary report.

d. For routine operations:

i. State whether the (b) (4) is monitored and describe the procedure? Please justify your response.

ii. Describe the environmental monitoring with justification for viable and non-viable, sampling locations, frequency and duration of sampling.

12. You provided the results of media fill simulation for Line-(b) (4) in the BLA submission. As this is a new filling line, please provide the protocol and results for the aseptic media simulations to include interventions, duration, personnel, etc...

13. You clarified during the June 10 telecon that the (b) (4) is validated for (b) (4) (to include several filling operations) between (b) (4). You added that the (b) (4) hold time was validated by at least (b) (4) media simulation runs – (b) (4). Please state the number of filling operations that can be performed during the (b) (4) and provide the studies performed to demonstrate that you have validated status support filling that number of lots. Please justify your response.

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 July 8, 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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