

From: Wittig, Anja <anja.wittig@octapharma.com>
Sent: Thursday, 28 June, 2018 02.33
To: Levi, Mark
Cc: Ammons, Stanley; Rangetiner, Barbara
Subject: RE: FDA IR for BLA 125587

Sensitivity: Confidential

Dear Mr. Levi,
We herewith confirm receipt of this email.

Kind Regards,
Rita Gorsche

On behalf of
Anja Wittig
Manager
International Regulatory Affairs Department

Octapharma Pharmazeutika Prod.ges.m.b.H. | Oberlaaer Strasse 235 | A-1100 Vienna Austria |
Office: +43 (0) 1 610 32 1707 | Fax: +43 (0) 1 610 32 9122 | anja.wittig@octapharma.com
| www.octapharma.com

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From: Levi, Mark [mailto:Mark.Levi@fda.hhs.gov]
Sent: Tuesday, June 26, 2018 3:02 PM
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. You provided in response to CR letter the Qualification/Validation of CCIT using the (b) (4) at OSA Lingolsheim (Report 705VAL193 CCIT (b) (4)). However, it is not clear why this study was submitted, considering that the OSA Lingolsheim facility “will only perform manufacturing from plasma to bulk solution ((b) (4))”. Lingolsheim (OSA) manufacturing facility is withdrawn as filling site for Panzyga bulk solution”, and no CCIT is performed at OSA Lingolsheim to support the

approval of this BLA. Please clarify.

We recommend that the validation of CCIT using the (b) (4) at OSA Lingolsheim be withdrawn from the current BLA submission. The CCIT validation at the OSA Lingolsheim facility should be resubmitted in the PAS to support the filling operations for Panzyga at OSA Lingolsheim.

2. You listed in Annex 1 the major manufacturing equipment, the respective manufacturing steps, and the qualification/cleaning/sterilization reports (where applicable).

Some of the vessels are used in several manufacturing steps. Per your protocols, the cleaning validation should verify cleaning following placebo and product/intermediate runs. For each vessel that is used for more than one manufacturing step, please list the intermediates/ products used for soiling the vessels (and the respective steps) prior to the cleaning validation run to ensure that cleaning validation was performed following each intermediate/product that comes in direct contact with the equipment. Please justify your response.

3. During review of the cleaning validation reports, we identified several points that need clarifications. Please provide clarification and additional information with justification for the reports listed below:

a. 751RQP002/01, Periodic Revalidation report following the cleaning of the (b) (4) material with the (b) (4) (approved 07 Dec 2015). You reported that the acceptance criterion for (b) (4) sampling ((b) (4)) varies depending on equipment/soiling material. However, you reported in other cleaning validation and procedures that the acceptance criterion is (b) (4). Please clarify.

b. 751RQP186/00, Requalification Report for (b) (4) of the tank (b) (4) (approved 31 Aug 2017). The previous validation report 751RQP030/02, included revalidation of the (b) (4) for tanks (b) (4) during production and was approved 13 March 2015. Please clarify why the current revalidation only included tank (b) (4), and there was no other revalidation submitted/performed for tanks (b) (4). Please justify your response.

c. 751RQP198/00, Validation Report for the Manual Cleaning of the filter (b) (4), Optimization of the cleaning method (modification of the order of cleaning sequences) (approved 12 Jan 2018).

i. You reported that the manual cleaning was modified (because of a deviation), by changing the cleaning sequence. Would that modification be applicable to Filter (b) (4) and Filter (b) (4)? Please explain.

ii. You reported results of (b) (4) sampling for the cleaning revalidation of Filter (b) (4) (report 751RQP033/02), but not for Filter (b) (4) (report 751RQP198/00). Please explain.

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 6, 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 Aug. 2, 2018.

Regards, Mark Levi
Mark Levi, PhD
Regulatory Project Management Staff
Center for Biologics Evaluation and Research
Office of Tissues and Advanced Therapies
U.S. Food and Drug Administration
Tel: +1 (240) 402-9662 Mobile +1 (301) 908-5787
mark.levi@fda.hhs.gov

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