

From: Thompson, Edward
Sent: Friday, May 22, 2015 11:25 AM
To: 'Kevin Darryl (KD) White (Kevin.White@cslbehring.com)'
Cc: Monica.Richardson@cslbehring.com
Subject: Information Request for BL 125582/0

Contacts: Kevin Darryl (KD) White - CSL Behring

Dear Mr. White:

We are reviewing your December 5, 2014 biologics license application (BLA) for Coagulation Factor IX (Recombinant), Albumin Fusion Protein. We determined that the following information is necessary to continue our review:

1. You only provided clearance studies on (b) (4), which is insufficient for the validation of clearance for non-enveloped viruses. Murine minute virus (MVM) is a relevant non-enveloped virus to the CHO cell line used for the production of Coagulation Factor IX (Recombinant), Albumin Fusion Protein. Please expand your validation studies to include MVM regarding the capability of the manufacturing process for viral clearance, such as the (b) (4)
2. (b) (4) test is performed for the (b) (4) in the production scale as indicated on Table 4, page 20 of 29 in the study DSVR-809-002-01 *Validation of the down-scale design for the virus filtration process step for RIX-FP*. However, this test was not included as an In-Process Control (IPC) in the production scale in Section 3.2.S.2.4.1 *Control of Critical Steps*. To be consistent, please add this test to be an IPC at (b) (4) Filtration on Table 3.2.S.2.4.1-2 in Section 3.2.S.2.4.1.
3. On Page 3 of 9 in Section 3.2.S.2.4.1 *Control of Critical Steps*, you did not include (b) (4) Solvent/Detergent to be critical process parameters at Step (b) (4) *Solvent-detergent virus inactivation*. As the data in your viral clearance studies indicate, these parameters are critical regarding virus inactivation. Please add these parameters with their acceptance limits to Table 3.2.S.2.4.1-1 *Critical Process Parameters for the Manufacture of the Drug Substance*.



125582.1_Origina...

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 June 30, 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.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is December 5, 2015.

Please send an acknowledgement for receipt of this request.

If you have any questions, please contact me at (240) 402-8443.

Sincerely,

Edward Thompson
Regulatory Project Manager
FDA/CBER/OBRR/RPMS

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone and return it to us at the above address by mail. Thank you.



Our Reference: BL 125582/0

CSL Behring Recombinant Facility AG
Attention: Mr. Kevin D White
May 22, 2015
Sent by email

Dear Mr. White:

We are reviewing your December 5, 2014 biologics license application (BLA) for Coagulation Factor IX (Recombinant), Albumin Fusion Protein. We determined that the following information is necessary to continue our review:

1. You only provided clearance studies on (b) (4), which is insufficient for the validation of clearance for non-enveloped viruses. Murine minute virus (MVM) is a relevant non-enveloped virus to the CHO cell line used for the production of Coagulation Factor IX (Recombinant), Albumin Fusion Protein. Please expand your validation studies to include MVM regarding the capability of the manufacturing process for viral clearance, such as the (b) (4)
2. (b) (4) test is performed for the (b) (4) in the production scale as indicated on Table 4, page 20 of 29 in the study DSVR-809-002-01 *Validation of the down-scale design for the virus filtration process step for RIX-FP*. However, this test was not included as an In-Process Control (IPC) in the production scale in Section 3.2.S.2.4.1 *Control of Critical Steps*. To be consistent, please add this test to be an IPC at (b) (4) *Filtration* on Table 3.2.S.2.4.1-2 in Section 3.2.S.2.4.1.
3. On Page 3 of 9 in Section 3.2.S.2.4.1 *Control of Critical Steps*, you did not include (b) (4) of Solvent/Detergent to be critical process parameters at Step (b) (4) *Solvent-detergent virus inactivation*. As the data in your viral clearance studies indicate, these parameters are critical regarding virus inactivation. Please add these parameters with their acceptance limits to Table 3.2.S.2.4.1-1 *Critical Process Parameters for the Manufacture of the Drug Substance*.

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 June 30, 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.

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is December 5, 2015.

Please send an acknowledgement for receipt of this request.

If you have any questions, please contact me at (240) 402-8443.

Sincerely,

Edward Thompson
Regulatory Project Manager
FDA/CBER/OBRR/RPMS