



Our Reference: BL 125488/0

Instituto Bioclon, S.A. de C.V.
Attention: Ms. Jennifer Spinella
April 8, 2013
Sent by facsimile

Dear Ms. Spinella:

We are reviewing your March 16, 2013 biologics license application (BLA) for Crotalidae (pit viper) Immune F(ab')₂ (Equine) Injection. We are providing the following comments and request for additional information to continue our review:

The following request for information pertains to review issues only:

Module 1 Contents

1. Please amend your request for a categorical exclusion. The request was made under the correct exclusion, 21 CFR 25.31 (c); however, the wording accompanying the request was incorrect.
2. The following hyperlinks appear to be broken:
Section 3.2.S.2.4 has a hyperlink to Section 3.2.R Executed Batch Records
Section 3.2.S.2.5 has a link to 3.2.S.4.4 Batch Analysis

Module 2 Contents

3. It is unclear if all applicable facility and equipment information is included in the submission. A list of equipment and utilities was supplied for the Tlalpan facility; however only a list of utilities was included in the submission for the (b) (4) facility. Please provide a list of all major equipment used in the (b) (4) facility for the fill finish of the Anavip drug product and indicate if the equipment is shared or dedicated to Anavip.

Module 3 Contents: Drug Substance

4. The (b) (4) bulk drug substance is shipped to (b) (4) for final fill and finish. Please provide the shipping validation for shipping of (b) (4) bulk drug substance from Tlalpan to (b) (4). Please include a description of the packing and shipping procedures.

Module 3 Contents: Drug Product

Container Closure

5. Please provide additional information on the stoppers and vials used as the container closure for the final drug product such as line drawings with measurements indicated. Please provide the acceptance specifications for the materials. Please provide a description for the process for the receipt of these materials. Is any testing conducted prior to release into production? Please provide a brief description of raw material qualification performed for these materials.

Process

6. Please confirm the manufacture of the bulk drug substance will only occur in the Talpan facility and the filling and lyophilization will only occur in the (b) (4) facility.
7. Please provide a description of the receipt process of the bulk drug substance at (b) (4). Please indicate where the material is stored and under what conditions.
8. Please describe the process for transferring the bulk drug substance to the filling machine; specifically, describe the container for the BDS and how it is connected to the filling machine. For example, is the BDS in a tank and then an aseptic or sterile connection is made from the tank to the filling machine?
9. Please provide a more detailed description of the types of gowning used and of the gowning process prior to entrance into the aseptic filling area.
10. Please clarify (b) (4) [REDACTED]. If this is not included in the media simulations, please provide the rationale for not including this step.
11. Please clarify where labeling of the vials will occur. Please describe the labeling process and the vial visual inspection process.

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 May 6, 2013 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 March 18, 2014.

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 immediately notify us by telephone and return it to us at the above address by mail.
Thank you

Please send an email message acknowledging receipt of this request.

If you have any questions, please contact me at (301) 827-9167.

Sincerely,

Edward Thompson
Regulatory Project Manager
FDA/CBER/OBRR/DBA/RPMB

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 immediately notify us by telephone and return it to us at the above address by mail.
Thank you