

From: Thompson, Edward
Sent: Friday, June 21, 2013 9:23 AM
To: 'Jennifer Spinella (jspinella@raretx.com)'
Cc: Kirschbaum, Nancy (Nancy.Kirschbaum@fda.hhs.gov); Waites, Nancy
Subject: Information Request for BL 125488/0

Contacts: Jennifer Spinella

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:

Drug Substance

1. The equipment information provided in the BLA was for the equipment qualification studies from 2009 – 2010. Please provide the most recent requalification summary reports for the following equipment to demonstrate the equipment has been run in a controlled manner and as qualified. Please include in the summary acceptance criteria and discuss any deviations that occurred, if applicable.
 - a. Depyrogenation Oven, Oven No (b) (4); specifically, the load pattern used for the depyrogenation of the (b) (4) used to hold the (b) (4)
 - b. Autoclave Type (b) (4) specifically, the load pattern(s) for the (b) (4)
2. Please indicate if there have been any changes to the equipment cleaning procedures since cleaning was initially validated.
3. Please provide a list of other products manufactured in the Tlalpan facility and indicate if the equipment used in the manufacture of Anavip is dedicated or shared.
4. The utility information provided in the BLA was for qualification studies performed in 2009 – 2010. Please provide the following information, since 2012, to demonstrate the facility and utilities have been run in a controlled manner and as qualified:
 - a. Summary of EM data for the manufacturing rooms and aseptic area including a summary of any major deviations and their investigation. Please include acceptance criteria.
 - b. Summary of testing results for the (b) (4) water used in manufacturing including a summary of any deviations and their investigations. Please include acceptance criteria.
5. Please list any changes or improvements in the manufacturing processes or facility for the manufacture of the (b) (4) bulk drug substance since 2011.

6. Please provide a short description for the procedure for receipt and storage of the horse plasma at the Tlalpan facility.
7. The (b) (4) is manufactured at the (b) (4) for use throughout the manufacturing process. Please provide the following information:
 - a. Description of the tank used to hold the (b) (4)
 - b. A summary of the tank cleaning and sterilization validation including any deviations and investigations, if applicable
 - c. Summary of the qualification studies for the expiration date of the (b) (4)
 - d. Summary of the procedure for (b) (4)
8. In Stage (b) (4), the description in the BLA states that (b) (4). This step does not appear to be captured in either the English translation of the BPR or the Spanish BPR which is actually used in production. Please indicate where in the BPR this step is captured. In addition, please provide additional information on tank (b) (4) specifically:
 - a. A description of the tank
 - b. A summary of the cleaning and sanitization/ sterilization qualifications
9. In Stage (b) (4) of the (b) (4) step a (b) (4) test is performed on the filter system; however the description of the test seems to refer to a (b) (4) test as opposed to a (b) (4) test. Please comment.

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 15, 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.

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

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