

From: Thompson, Edward
Sent: Thursday, April 18, 2013 7:43 AM
To: 'Jennifer Spinella (jspinella@raretx.com)'
Cc: Kennedy, Michael; Virata, Maria Luisa
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:

Raw Materials

1. Please provide representative Certificates of Analysis (CoA) from each supplier/manufacture for the following manufacturing process reagents: (b) (4) sodium chloride, (b) (4), and (b) (4). If different grades of sodium chloride are used for each process step, please provide the CoA for each type.
2. There were a few CoAs you submitted that were listed as being from (b) (4)". Please confirm whether this is a typographical error and that the correct manufacturer's name should be (b) (4).
3. There were some discrepancies regarding the names of the suppliers/manufacturers you listed in Table 1: List of Reagents used in the Production of Anavip (Section 3.2.S.2.3 Control of Materials) vs. the names on the actual representative CoAs you provided. For instance, you indicated that your supplier for several reagents is (b) (4) and yet the representative CoAs you submitted are from (b) (4). For other reagents, you listed (b) (4) as the supplier, however, the CoAs were again from (b) (4). There were also CoAs listed as being (b) (4)", but the corresponding supplier on your table is (b) (4). Please clarify the following:
 - a. Why several CoAs were from (b) (4) and not the listed supplier/manufacture
 - b. What is the relationship between (b) (4)
 - c. What is the relationship between "(b) (4)
 - d. What is the relationship between (b) (4)
4. Please provide a representative CoA from your (b) (4) supplier of the (b) (4) snake venoms (if available).

Product (b) (4)

5. Your proposed (b) (4) [redacted] which indicate to us that you do not have good control of your manufacturing process. (b) (4) [redacted] to reflect the capacity of the manufacturing process. (b) (4) [redacted] production lots of Anavip and/or identically manufactured products with different specificities.
6. Please establish a (b) (4) [redacted] in the Anavip final product based on data of Anavip lots tested by a validated (b) (4) [redacted]. Please include the statistical analysis report from testing a sufficient number of Anavip final product lots to support your (b) (4) [redacted].

Adventitious Agents Testing

7. Your current method SOP for (b) (4) [redacted] testing of adventitious agents in horse plasma lacks the follow-up tests recommended in 9 CFR §113.53 (c)(6) for the detection of cytopathogenic and/or hemadsorbing agents (as prescribed in 9 CFR §113.46) and the detection of extraneous viruses by the fluorescent antibody technique (as prescribed in 9 CFR §113.47). Please provide your method SOPs and method validation study reports for these additional tests, if available.

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 2, 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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