Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

To:	File for 125335
From:	Joel J. Beren DVM, Deputy Director, Division of Veterinary Services DVS/OM/CBER
Through:	Philip J. Snoy DVM, Director, Division of Veterinary Services DVS/OM/CBER
CC:	Robert W. Fisher, Chair of the Review Committee
Product:	Centruroides (Scorpion) Immune $F(ab')_2$ (Equine) Injection "Anascorp"
Subject:	Veterinarian consult review for STN 125335/0, Centruroides (Scorpion) Immune $F(ab')_2$ (Equine) Injection, "Anascorp"

Recommendation:

Approval.

Executive Summary:

RDT/Bioclon ----------

----------(b)(4)----------

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Background:

1. In January 2009, Instituto Bioclon, S.A. de C.V. submitted an original BLA for a lyophilized $F(ab')_2$ product manufactured from equine plasma.
    a. On 30 January 2009, the submission chair, Dr. Robert W. Fisher, requested a veterinarian consult for animal husbandry procedures, to include horse vaccination and bleeding procedures.
    b. I was assigned the consult on 5 February 2009 by Dr. Philip J. Snoy.
    c. The submission chair provided the relevant animal husbandry sections from the BLA, as well as the preBLA minutes, on 20 February 2009.
2. ----------(b)(4)----------.
    a. ----------(b)(4)----------.
    b. ----------(b)(4)----------.

c. ----------(b)(4)----------.

i. ----------(b)(4)----------.

3. ----------(b)(4)----------.

a. ----------(b)(4)----------.

b. ----------(b)(4)----------.

4. ----------(b)(4)----------.

5. ----------(b)(4)----------.

a. ----------(b)(4)----------.

b. ----------(b)(4)----------.

c. ----------(b)(4)----------.

6. Several issues were noted in the initial review involving the blood/serum collection procedure, horse procurement and husbandry, horse prophylactic immunization, and venom immunization procedures. See Appendix B.

a. An information request was submitted to the sponsor on 14 April 2009 in order to clarify animal husbandry issues. Bioclon submitted a response dated 1 May 2009 (STN 125335/0.22).

b. In general, the responses were acceptable. However, the following items remained unresolved and were included in the CR letter issued 23 July 2009:

- Please submit and implement plasma screening procedures, such as those described in 9 CFR 113.53, to preclude introduction of adventitious agents into your manufacturing stream. You may do this on the plasma pool in lieu of testing individual plasma units.

- In the absence of adequate data to validate cleaning and sterilization for the needle and tubing set used in bleeding your donor herd, you should use a new sterile disposable hypodermic needle and sterile disposable IV collection set for each bleed. Please implement this change and submit a revised SOPP.

- Given the excessive bleed volumes and aggressive bleeding schedule, we very strongly recommend that you measure and document the hematocrit of donor horses prior to each bleed and 2-3 days post-bleed. You should not bleed animals with hematocrits below 25% . Hematocrits should not drop below 18% post-bleed. This information should be recorded in the veterinary records for each horse.

- ----------(b)(4)----------.

- Please establish a quality assurance certification program to include hay, pelleted feed, and water. You should monitor the water source for your donor animals to ensure sufficient quality; an annual report from the municipal water supplier may be sufficient if contaminants, such as toxic organic compounds (e.g., herbicides and pesticides), in use in the region are monitored. Please submit your certification program and relevant data.

- Please verify that your SOP P-SA-029 establishes adequate withdrawal times for each therapeutic used for treatment of your donor herd. Please submit the revised SOPP to reflect these times.

- We acknowledge your response of May 1, 2009, that indicates you will immunize horses against ----------(b)(4)----------. Please verify that you will manufacture lots of your product designated for the U.S. market using plasma from vaccinated horses. You should provide immunization protocols to include doses, immunization frequency, and deferral times for horses after immunizations. We will verify immunization records on inspection.

7. A response to the CR was received on 1 February 2011; this included a change in sponsor from Bioclon to Rare Disease Therapeutics, Inc (RDT). The animal husbandry CR items were reviewed and are summarized below:

    a. ----------(b)(4)----------.

    b. ----------(b)(4)----------.

    c. RDT agreed to monitor --(b)(4)-- in production horses. The testing/bleeding scheme is presented in **Error! Reference source not found.**, below. --(b)(4)-- data was also provided for two groups of Anascorp horses.

    d. ----------(b)(4)----------.

    e. RDT established a QA certification program for food and water monitoring, as described in 2.a above.

    f. RDT submitted SOP P-SA-029, ----------(b)(4)----------.

    g. RDT provided details of the ----------(b)(4)---------- vaccination program for the donor herd. See **Error! Reference source not found.**, below.

Tables and Figures:

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