



Official Meeting Summary

Meeting ID #: CRMTS #7517
Application type and number: BLA 125335/0
Product name: Centruroides (Scorpion) Immune F(ab')₂ Intravenous (Equine)
Sponsor or Applicant: Bioclon, S.A. de C.V.
Meeting type: Type C
Meeting category: BLA, Other
Meeting date & time: July 15, 2010 11:30 a.m. –11:45 a.m.
Meeting format: Teleconference
Meeting Chair/Leader: Dorothy Scott, M.D.
Meeting Recorder: Debbie Cordaro and Philip Yoo

FDA Attendees:

Dorothy Scott, M.D., Chief, Lab. of Plasma Derivatives, Division of Hematology, OBRR
Michael Kennedy, Ph.D., Team Leader, Division of Hematology, OBRR
Robert Fisher, Ph.D., Staff Fellow, Division of Hematology, OBRR
Nancy Waites, Biologist, Division of Manufacturing and Product Quality, OCBQ
Lori Peters, Consumer Safety Officer, Division of Manufacturing and Product Quality, OCBQ
Mahmood Farshid, Ph.D., Deputy Director, Division of Hematology, OBRR
Phillip Yoo, Contractor, Division of Blood Applications, OBRR
Debbie Cordaro, Regulatory Project Manager, Division of Blood Applications, OBRR

Instituto Bioclon, S.A. de C.V. (Bioclon) Attendees:

Juan Lopez de Silanes, Ph.D., President, Instituto Bioclon, S.A de C.V.
Jorge F. Paniagua, Ph.D., Vice President, Instituto Bioclon, S.A de C.V.
Walter Garcia Ubbelohde, M.D., Medical Director, Instituto Bioclon, S.A de C.V.
Rita Mancilla Nava, Plant Manager, Instituto Bioclon, S.A de C.V.
Milton Ellis, President, Rare Disease Therapeutics, Inc.
Chip Perry, Clinical Manager, Rare Disease Therapeutics, Inc.
Jude McNally, Pharm.D., Director, Medical Science Liaison, Rare Disease Therapeutics, Inc

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Jennifer Spinella, MT(ASCP), RAC, ----- (b)(4) -----

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Background and Objectives:

On January 21, 2009, Instituto Bioclon, S.A. de C.V. (Bioclon) submitted a biologics license application (BLA) for the use of Centruroides (Scorpion) Immune F(ab)₂ Intravenous (Equine) in the treatment of clinically important signs of scorpion envenomation. On July 23, 2009 FDA issued a complete response (CR) letter. Bioclon submitted this meeting request/meeting package as an amendment to their BLA on May 6, 2010. The purpose of the meeting is to discuss

chemistry, manufacturing and controls issues (CMC) particularly related to process validation and clinical issues. On June 3, 2010 a telecon was held to discuss the clinical question submitted in this meeting request. No further discussion about the clinical issue is needed during this meeting.

FDA provided their preliminary responses to the applicant on July 12, 2010. After reviewing the proposed responses, Bioclon notified FDA on July 12, 2010 of their decision to proceed with the meeting.

Discussion

Introductions were made. FDA noted that the clinical issue had been discussed and resolved during a teleconference held June 3, 2010. Regarding the CMC comments, Bioclon will make the changes recommended by FDA, however, they requested further discussion of item 2 in the first paragraph of our response.

Chemistry, Manufacturing and Controls (CMC):

Sponsor/Applicant Question 1:

Enclosed are the Process Validation Protocol, Process Validation Report, Master Batch Production Record and a Technology Transfer Protocol. Three Anascorp batches were produced in the Instituto Bioclon Tlalpan manufacturing plant using the processes defined within these documents.

In addition, the Technology Transfer Protocol was developed as a result of the Pilot Plant production and report and will be utilized to produce three lots in the commercial manufacturing facility.

Does the Agency have any comments to the Protocol and Validation Report?

FDA Response to Question 1:

FDA recognizes Instituto Bioclon's progress in addressing the issues in the Complete Response letter. We recommend 1) modifications to the Master Batch Record as noted below and in the Complete Response letter, 2) performing PV/engineering runs using -----(b)(4)----- plasma after the full scale tech transfer and prior to the conformance lots, and 3) scheduling the final conformance lot to coincide with the FDA inspection.

FDA is unable to provide comprehensive comments to the information provided since it would be more appropriate to review it as a response to the CR letter. Reviewing documents out of context is not an appropriate practice since the validation of a process not only includes the process itself, but also equipment, personnel, facilities, media challenges, etc.

FDA requests that you be prepared to discuss the following during our teleconference:

The question submitted by Bioclon to the Agency is very broad and general; therefore, we are unable to provide a comprehensive response to the question posed. Please be

prepared with specific comments or concerns related to the Protocol and Validation Report that was submitted as pre-read material.

Appendix 11 – Please clarify the purpose of this appendix. FDA is unable to determine what the information provided is supporting or what conclusion is expected to be drawn from the inclusion of this information.

Filling Batch Production Record: In the batch record, the operator is instructed to

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We have the following comments for inclusion in your response to the Complete Response letter:

- Appendix 5 Part 2 Pg 171 Filler (b)(4) Performance Qualification Report – It appears Bioclon is continuing to average a failing result with passing results. Please reference the Form FDA 483 # 20b.
- Appendix 5 Part 2 Pg 172-174. The Comments Section states “cancelled.” Please clarify what this means.
- It does not appear that Bioclon included Process Step Time limitations in their BPRs. Please reference Form FDA 483 #2.

Specific comments related to the master batch record used for production of your pilot lots are provided below. We note that some, but not all, of these concerns have been addressed in the updated master batch record as described in the technical transfer protocol.

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Discussion:

FDA recommended Bioclon perform PV/engineering runs using -----(b)(4)----- plasma after the full scale tech transfer and prior to the conformance lots. This would be an opportunity to practice producing a full-scale run before manufacturing the conformance lots and will facilitate identifying potential gaps in the batch record. Since -----(b)(4)----- plasma would be similar in protein concentration and other parameters (except potency) it would allow a more cost-effective evaluation of the process while minimizing loss of valuable ----(b)(4)---- plasma. However, Bioclon may choose to use ----(b)(4)---- plasma instead of -----(b)(4)----- plasma for the engineering runs if they so desire. Bioclon expressed concern about the availability of -----(b)(4)----- plasma, and inquired if it were permissible to use ----(b)(4)---- plasma from horses immunized against non-scorpion related antigens. FDA responded that provided the plasma is otherwise equivalent to anti-coral plasma and meets the same testing criteria as for anti-coral plasma, either -----(b)(4)----- plasma or other ----(b)(4)---- plasmas may be used for the engineering runs.

Bioclon confirmed that the process will be validated at the -----(b)(4)----- scales. They also clarified that the full scale tech transfer runs would not be considered as conformance lots and that one lot would be manufactured during the FDA prelicensure inspection.

Bioclon is anticipating implementing these runs at the beginning of September and the review of the data should be completed by the end of December. They anticipate a resubmission date and response to the 483s by February 1, 2011. The end of September 2010 would be the cut-off data for the clinical data.

The Food and Drug Administration Amendments Acts (FDAAA) allow for FDA to withdraw a submission if a year has lapsed since the issuance of a Complete Response (CR) letter. FDA clarified that the one year timeline is for submissions where FDA is unaware of any initiative to address the complete response letter and does not apply due to the ongoing interactions between FDA and Bioclon to facilitate licensure.

Decisions made and/or agreements reached:

None

Issues requiring further discussion:

None

Action items:

None

Attachments/Handouts:

None

END