DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
1401 Rockville Pike
Rockville, MD 20852-1448

Meeting Response Memorandum

Our Reference: CRMTS #7517
Ref. # STN 125335/0

Division of Blood Applications

TODAY'S DATE: July 12, 2010 PAGES: # 5

TO: ----------(b)(4)----------
Instituto Bioclon, S.A. de C.V.
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Email address:----(b)(4)----

FROM: Debbie Cordaro
Regulatory Project Manager
Division of Blood Applications
OBRR
Phone number: (301) 827-6157
Fax number: (301) 827-2857

SUBJECT: Summary of FDA Internal Meeting

PRODUCT: Centruroides (Scorpion) Immune $F(ab')_2$ Intravenous (Equine)

We completed our review of your information package for Centruroides (Scorpion) Immune $F(ab')_2$ Intravenous (Equine) and are providing the following responses to the questions you posed in the package. Although we continue to reserve July 15, 2010 11:30 a.m. – 1:00 p.m. Eastern for a telecon with you regarding this product, if you find that our attached responses and advice are sufficiently clear and complete to obviate the need for further discussion, please inform us as soon as possible so that we may clear the meeting time. Alternatively, if you have questions regarding specific responses or advice, please inform us so that the appropriate members of the review team can provide clarification during the reserved meeting time.

THANK YOU

Questions from Instituto Bioclon:

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 Biocl6n 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, and 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.

The Agency 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 contexts 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. I am unable to determine what the information provided is supposed to support 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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----------(b)(4)----------. How does Bioclon determine when the fill volume was inaccurate and how many vials it affects?

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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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Clinical

Sponsor/Applicant Question 1:

Cutoff Date/Update of Ongoing Clinical Study

FDA acknowledged that it would take time for Bioclon to organize data to update the safety database for AL-03/07 clinical study and to also update the Integrated Summary of Safety. The Agency tentatively agreed with Bioclon's proposed date for data cutoff as June 2009. However, FDA subsequently determined that it is not reasonable to set a cutoff date ahead of knowing Bioclon's timeline for responding to the complete response (CR) Letter. Thus, FDA included in the minutes to the teleconference this Post-Meeting Comment:

> "If the date of resubmission is delayed, the cutoff date for the integrated safety report must be adjusted to no more than 90 days prior to resubmission. Should Bioclon have difficulty in meeting this cutoff, please explain in detail your needs in organizing the additional safety data for resubmission in response to the CR Letter, and how that will impact the time frame for data cutoff. .. "

Bioclon will be able to provide a safety update as requested by FDA, however it would be extremely difficult if not impossible (see below) for Bioclon to adjust the cutoff date for integrated safety data to no more than 90 days prior to resubmission. Working with the data management group and collecting all new CRFs from the sites (approximately 24) takes considerable amount of effort and time. Subsequently, once all data is available, new tables and listings must be generated. It is not possible for this task to be completed 90 days prior to the submission of Bioclon's response to the Agency's CR letter. We request a 180-day time period.

Please note that the safety database for this product has become much larger than originally planned due to continuation of study AL-03/07 out of compassion to these patients during the BLA review phase. The Agency will now have data on over 800 patients and there have been no significant safety signals. Thus, as noted above Bioclon's request is to collect data up to 180 days prior to resubmission, prepare a response as requested by FDA and submit this information in Bioclon's response to the Agency's CR letter.

Does the Agency agree with this proposal?

FDA Response to Question 1:
This issue was resolved with Bioclon during a teleconference held June 3, 2010.

END