



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

Date: June 20, 2009

To: STN: 125335.0

From: Pei Zhang, MD, Division of Hematology (DH), OBRR, HFM-345

Through: Mei-ying, W. Yu, Ph.D. DH, HFM-345
Dorothy Scott, M.D., LPD Chief, DH, HFM-345

CC: Debbie Cordaro RPM, HFM-370

Applicant: Instituto Bioclon

Product: Centruroides (Scorpion) Immune F(ab)₂ Intravenous (Equine)
Trade name: Anascorp[®]

Subject: Final Review

Recommendation

The study for viral validation for Anascorp[®] needs to be complete. A complete response letter will be sent to the sponsor with the following questions regarding virus validation.

1) Please complete the small-scale validation studies of the nanofiltration step with the consideration of mimicking the full scale manufacturing process. If there is an unavoidable difference, please justify it and verify the difference does not compromise the validity of small scale studies. The validation studies should include the clearance of enveloped viruses and non-enveloped viruses, for example, XMuLV, PRV and PPV. Critical parameters related to the full scale manufacturing process should be monitored during the validation studies. These parameters, such as----- (b)(4) -----, should be used to define your small scale viral validation studies.

In addition, please note that filter integrity is an essential in-process control and that the performance of the filter used in your viral validation studies must be compared to that of the filters used in your full scale production. Please note that Bioclon was informed in the CMC pre-BLA meeting of 08 Jan 2008 that with regards to non-enveloped virus, for example, PPV, "testing results must be provided to assess removal of small viruses." Also note that ICH guidance Q5A indicates that "viral clearance characterization studies should be performed with nonspecific model viruses with differing properties"

2) Inactivation curves are critical since virus inactivation does not follow simple first-order kinetics. Please provide kinetic data on inactivation of your model viruses such as ----- (b)(4) -----

(b)(4)

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These data appear to be supportive. However, there are no data provided for the evaluation of the robustness of these steps. Data obtained from kinetic studies under worst-case conditions should be provided. Therefore, the virus validation is incomplete.

(b)(4)

Reviewer's comments:

These data appear to be supportive. However, there are no data provided for the evaluation of the robustness of these steps. Therefore, the virus validation is incomplete.

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No robustness data are provided. The validation of virus clearance could not be demonstrated.

