



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

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**To:** BLA STN 125335/0

**Cross Reference:** IND (b)(4)

**From:** Evi Struble, Ph.D.

**Through:** Dorothy E. Scott, M.D.

**CC:** Debra Cordaro, RPM, HFM-370

**Applicant:** Instituto Bioclón S.A. de C.V.'s

**Product:** Anascorp®, Centruroides (Scorpion) Immune F(ab')<sub>2</sub> Intravenous (Equine)

**Subject:** Review of Amendment 0.24 Received on 06/18/2009 in Response to the Information Request Dated 06/10/2009

**Brief Description of the Amendment**

The sponsor was contacted with questions regarding the GLP animal study submitted and a toxicity assessment of the impurities present in the final product. Below is a review of the responses.

1. Animal study number: 1299-001 (Acute Toxicology Study in Rats)

Questions were aimed at ascertaining that the intended systemic exposure with the biologic was achieved which would allow to set a NOAEL in rats. The answers submitted clarified that systemic exposure in any of the dose groups was not achieved after dosing the subjects with a very concentrated solution of Anavip. As a result, this reviewer concludes that the data from this animal study cannot be used to make any label claims regarding the safety of this product in animals. However, based on the experience with this product in human subjects, it is not useful to perform additional animal studies at this time.

2. Toxicity assessments for cresol ---(b)(4)---  
Cresol

The reviewer does not agree with sponsor's conclusions of several orders of magnitudes high safety margins. We based our calculations on the final specifications of the product, namely Cresol -----(b)(4)----- which is equivalent to -----(b)(4)----- . The exposure for cresol from one 5 mL vial would be --- (b)(4) --- and from 5 vials would be --(b)(4)--. This amount of exposure would be similar to the daily exposure from other licensed products containing label warning about cresol.

Sponsor makes the wrong calculations and uses the wrong units equating --(b)(4)-- with --- (b)(4) ---, when in fact is --- (b)(4) ---. Based on the batch data submitted with the amendment 0.24, Appendix 2 and your calculations on the "theoretical maximum level of cresol", please revise the specification for cresol downward.

-(b)(4)-

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**Letter ready comments:**

1. Based on the batch data submitted with the amendment 0.24, Appendix 2 where the measured amount of cresol is -----(b)(4)--- and your calculations on the "theoretical maximum level of cresol" being --- (b)(4) -----, please revise the specification for cresol downward from --- (b)(4) ----.
2. Please consider setting a separate specification for -(b)(4)- to reflect the amount present in the final formulation.