

**Memorandum of Filing: BLA STN 125488/0, Crotalidae (Pit-Viper) Immune F(ab')<sub>2</sub> (Equine) Injection**

DATE: May 2, 2013

FROM: Mitchell Frost, M.D., Medical Officer, CBER/DH/CRB, HFM-392

THROUGH: Nisha Jain, Chief, CBER/DH/CRB, HFM-392

TO: The File for BLA STN 125466/0

SUBJECT: Original BLA/Supplemental BLA Filing: Crotalidae (Pit-Viper) Immune F(ab')<sub>2</sub> (Equine), Instituto Bioclon S.A. de C.V.

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**Conclusion and Recommendation**

1. This application is fileable.
2. This application does not trigger PREA because the product has received orphan designation.

**Brief Description of BLA Submission**

This submission for a lyophilized antivenin formulation from Instituto Bioclon S.A. de C.V. has been submitted electronically in accordance to Guidance for Industry: Providing Regulatory Submissions to the Center for Biologics Evaluation and Research (CBER) in Electronic Format — Biologics Marketing Applications. The submission is also compliant with ICH guideline M4E, Common Technical Document for the Registration of Pharmaceuticals for Human Use, using appropriate numbering within the Modules. An Index provides links to the relevant sections. The submission contains the following:

<b><u>Files/Folders</u></b>	<b><u>Information</u></b>
Files	(a) Cover letter, (b) Form 356h, (c) Form 3674, (d) Reviewers Guide Module 1 for ICH CTD
Folders/ Files	<ul style="list-style-type: none"><li>• Labeling</li><li>• Debarment Certification</li><li>• User fee cover sheet - Form 3397</li><li>• Financial information</li><li>• Other Table of Contents</li></ul> Module 2 for ICH CTD <ul style="list-style-type: none"><li>• Summary</li><li>• ICH CTD Module 2.3 Quality Overall Summary</li><li>• ICH CTD Module 2.4 Nonclinical Overview</li><li>• ICH CTD Module 2.6 Nonclinical Written and Tabulated Summaries</li></ul>

- Module 3 Quality ICH CTD
- Module 4 Nonclinical Study Reports ICH CTD
- Module 5 for ICH CTD
  - Clinical information
  - Statistical information
  - Case report tabulations
  - Case report forms

The indication in the proposed package insert is “an antivenom indicated for the management of patients with North American crotalid envenomation regardless of severity, including the prevention of late or recurrent coagulopathies.”

Materials for Administrative/Labeling information as well as the Overviews and Summaries appear to contain the required information for review.

- **The proposed labeling (package insert) conforms to the PLR format under 21 CFR 201.57 (71 FR 3922-3997; January 24 2006), and has been provided in both annotated (in pdf) and clean (in Microsoft Word) versions. The SPL version has also been included.**
- **Financial certification and disclosure information (Form 3454) have been submitted. The applicant certifies that there have been no arrangements where the value of the compensation could have been affected by the outcome of the study. A list of Investigators for Study YA-07/02 is included in the Financial Information folder.**
- **There are no PREA requests because this product has received orphan designation.**

CMC and Nonclinical data (ICH CTD Modules 3 and 4) are to be reviewed by Robert Fisher.

The clinical study reports (ICH CTD Module 5) will be reviewed by me as the Clinical Reviewer, and by Mary Lin the Statistical, the Iftekhar Mahmood Pharmacokinetics, and Erin McDowell the BIMO Reviewers.

### **Clinical Information**

The clinical material is located in Modules 2 (2.5, 2.7) and 5:

- Module 2 contains the Clinical Overview (2.5) and Clinical Summary (2.7)
- Module 5 consists of the following sections:

<b><u>Volume(s)</u></b>	<b><u>Information</u></b>
5.2	List of clinical studies
5.3.3	YA-06-07-a phase 1 biosafety study and PK study of antipymyn [antivenin crotalinae (pit viper) equine immune f(ab) <sub>2</sub> ]
5.3.5	AN-03-02-a comparaisn of Anavip (Crotalinae [pit viper] equine immune f(ab) <sub>2</sub> ) and Crofab (Crotalidae polyvalent immune fab ovine) in the treatment of Crotalinae envenomation a randomized, prospective, open-label, controlled, comparative, multicenter study  YA-07-02-a comparison of Anavip (Crotalinae [pit viper] equine immune f(ab) <sub>2</sub> ) and Crofab (Crotalidae polyvalent immune fab ovine) in the treatment of Crotalinae envenomation a randomized, prospective, blinded, controlled, comparative, multicenter study
5.4	Literature references

The objectives and design of the clinical studies are adequate to potentially support licensure of the product for the requested indication.

**Comments**

1. The clinical safety and efficacy data in this application are based on trials in Crotalinae envenomated patients; these trials having been conducted under BB-IND 11275.

2. The information in this BLA has been submitted in electronic format. On its face, the submission contains the required sections of a BLA, and it is legible and well organized. The definitions in the datafiles have been provided.