

Memorandum

**Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality**

To: 125488/0 Crotalidae (pit viper) Immune F(ab')₂ (Equine) Injection; Anavip

Michael Kennedy, PhD, Chair, OBRR/DH/LPD/ HFM- 345

Edward Thompson, RPM, OBRR/DBA/RPMB/ HFM- 380

Cc: Review Committee Members

Michael Brony, OCBQ/DCM/APLB, Labeling, Promotional Materials

Robert Fisher, PhD, OBRR/DH/LPD, CMC, Product

Mitchell Frost, MD, OBRR/DH/CRB, Clinical

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From: Nancy Waites, CMC Facility Reviewer, OCBQ/DMPQ/B1

Through: Carolyn Renshaw, Branch Chief, OCBQ/DMPQ/B1

Through: John Eltermann, Division Director, OCBQ/DMPQ

Subject: Review of Response to Complete Response Letter

Indication: Management of patients with North American envenomation to include prevention of late and recurrent coagulopathies

Applicant: Instituto Bioclon, S.A. de C.V. U.S. License # 1900

Facility Sites: Instituto Bioclon, S.A. de C.V. (FEI: 3007581821), Tlalpan, Mexico

Instituto Bioclon, S.A de C.V; (b) (4) México

CR Response Review Memo Due Date Goal: 06 Apr 2015

Final Action Due Date: 06 May 2015

Recommendation: The responses to the CR letter are acceptable. I recommend approval of this submission if the Product Office does not have any issues.

Information Request Dates:

None

Telecon Dates:

None

Summary

On 18 Mar 2013 the FDA received an original Biologics License Application (BLA) submitted electronically in eCTD. A Complete Response letter was issued to Instituto Bioclon on 18 Mar 2014. Bioclon's response was received by the FDA on 06 Mar 2015. I have reviewed the information submitted and find it to be acceptable.

Noteworthy Aspects

None

Post Marketing Commitments

None

Review and Comment

The CR comments submitted by FDA are in **bold** font followed by Bioclon's response in *italic* font.

- 1. We are unable to complete the final approval action pending the review of the January 14-23, 2014 inspection of your Tlalpan, Mexico D.F., Mexico facility.**

Instituto Bioclon Response:

In response to the Complete Review Letter dated March 18, 2014, Instituto Bioclon S.A. de C.V. believes they have fulfilled all of the Agency's concerns.

- Responding to and addressing all items issued in the Warning Letter dated April 16, 2014. A response was submitted to FDA May 13, 2014.*
- Responding to and addressing all observations/483s issued during the January 14-23, 2014 FDA inspection of the Tlalpan, Mexico D.F., Mexico facility. A response was submitted to FDA February 12, 2014.*
- Responding to and addressing all observations/483s issued during the November 10-20, 2014 FDA inspection of the Tlalpan, Mexico D.F., Mexico facility. A response was submitted to FDA December 9, 2014.*

OCBQ/DCM is still reviewing the inspection reports and has not yet issued a close out letter to Bioclon/RDT.

Review Response: Per DCM, Instituto Bioclon in Tlalpan will have an acceptable Compliance Check.

2. Cleaning validation for the filling equipment is not complete. Please submit the final study for the cleaning validation in your complete response to this letter.

Instituto Bioclon Response:

- *The cleaning validation study for the filling equipment is completed and it is included in 3.2.A.1 Facility and Equipment; Equipment; (b) (4) Facility: cleaning-val-filling-anavip.*

Review Response: I reviewed the protocol and report for the filling of the filling line used at the (b) (4) facility and found it to be acceptable.

The information provided included the following documents:

- PMV-019 Cleaning Validation Master Plan for (b) (4) (English translation)
- PV410 Validation Protocol (English Translation) Cleaning Validation of Liquid Filler and Capping Machine Code: (b) (4)
- VAP-0056-14 Cleaning Validation Report (English Translation) Cleaning Validation of Liquid Filler and Capping Machine Code: (b) (4)

The original Spanish versions of the three documents listed above were also included in the response.

Bioclon performed three studies consisting of three fills of Anavip and a dirty hold time of (b) (4)

[Redacted]

(b) (4)

[Redacted]	[Redacted]	[Redacted]
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