

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

Erica Giordano, OCBQ/DMPQ/PRB, Other, Quality Control

Ravi Goud, MD, OBE/DE/AEB, Epidemiology

Xue Lin, PhD, OBE/DB/TEB, Biostatistics

Iftexhar Mahmood, MD, OBRR/DH, Clinical Pharmacology

Erin McDowell, OCBQ/DIS/BMB, BIMO

Evi Struble, PhD, OBRR/DH/LPD, Pharm/Tox

Maria Virata-Theimer, OBRR/DH/LPD, CMC, Product

Yonggang Wang, PhD, OBRR/DH/LPD, CMC, Product

Lilin Zhong, OBRR/DH/LPD, CMC, Product

From: Nancy Waites, CMC Facility Reviewer, OCBQ/DMPQ/B1/HFM-675

Through: Carolyn Renshaw, Branch Chief, OCBQ/DMPQ/B1/ HFM-675

Through: John A. Eltermann, Jr., R.Ph., M.S., Director Division of Manufacturing Product Quality

Subject: Addendum Review Memo

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) (FEI: Not issued yet), (b) (4)
México

Review Memo Goal Due Date: 14 Feb 2014

Final Action Due Date: 18 Mar 2014

Recommendation: DMPQ recommends approval of the application if no other members of the review committee have any issues. I have one PMC for the application.

Please include the following PMC in the final action letter:

Bioclon commits to performing cleaning validation for the filling equipment. This validation will be completed and the results will be submitted to the application as a PMC-Final Study Report no later than 29 August 2014. Routine testing of the (b) (4) for (b) (4) will be conducted in the interim until the study is completed.

Summary

Review Note: At the close out of this review memo, Bioclon has not provided an FEI number for their (b) (4) facility. They have a DUNS number, (b) (4) and they have registered with the FDA, but an FEI number has not been issued.

I have reviewed the amendments that are applicable to DMPQ's review of the application and I find them acceptable. I do not have any further question or comments. The responses to the 483 that was issued during the pre-license inspection, conducted (b) (4), were acceptable.

I held a telecon with Bioclon on 07 Jan 2014 to discuss their response to Observation #1 from the 483 and to discuss improving their batch production records for better documentation.

Please include the following PMC in the final action letter:

Bioclon commits to performing cleaning validation for the filling equipment. This validation will be completed and the results will be submitted to the application as a PMC- Final Study Report no later than 29 August 2014. Routine testing of the (b) (4) for (b) (4) will be conducted in the interim until the study is completed.

Telecons:

A telecon was held with Bioclon on 07 Jan 2014. The minutes of the telecon are uploaded into the EDR.

Review:

The following is a list of the information requests sent out by DMPQ over the course of the Primary Review of the BLA along with a list of the resulting amendments. The review of the BLA was managed under PDUFA V “The Program”.

IR Date	Amendment Number	Review Result
08 Apr 2013 (Issues could affect filing)	Amendment 6	Acceptable
08 Apr 2013 (General information request)	Amendment 8	Acceptable
21 Jun 2013	Amendment 14	IR sent 15 Nov 2013
17 July 2013	Amendment 16	IR sent 15 Nov 2013 Possible PMC
07 Oct 2013	Amendment 28	IR sent 15 Nov 2013
16 Oct 2013	Amendment 29	IR sent 15 Nov 2013
15 Nov 2013	Amendment 32	Acceptable – Resulted in PMC

The reviews of these amendments are attached to this addendum review memo as appendices.

List of Appendices

- Appendix 1 – Review of Amendment 6 - Responses to Information Request Dated 08 April 2013 for Issues that could affect Filing
- Appendix 2 - Review of Amendment 8 - Responses to Information Request Dated 08 April 2013 for Review Issues
- Appendix 3 - Review of Amendment 14 - Responses to Information Request Dated 21 June 2013
- Appendix 4 - Review of Amendment 16 - Response to FDA Information Request Dated July 17, 2013
- Appendix 5 - Review of Amendment 28 - Response to FDA Information Request Dated 07 Oct 2013
- Appendix 6 - Review of Amendment 29 Response to FDA Information Request Dated 16 Oct 2013
- Appendix 7 - Review of Amendment 32 - Responses to Information Request Dated 15 Nov 2013