



MEMORANDUM

Date: May 8, 2015

To: File for STN 125488/0

From: Karen Campbell, Regulatory Coordinator
Division of Biological Standards and Quality Control (DBSQC)

Through: William McCormick, Ph.D.
Director, Division of Biological Standards and Quality Control (DBSQC)

Subject: STN 125488 Crotalidae (pit viper) Immune F(ab')₂ (Equine) Injection review of the lot release protocol template

CC: Michael Kennedy
Hyesuk Kong
Cheryl Hulme
Catherine Poole

Background: Lot release protocol template

Submissions Reviewed in this Memo:

125488/0.23 Lot release protocol template
125488/0.31 Lot release protocol template
125488/0.35 Responses to our information request

Conclusion: The lot release protocol template submitted in 125488/0.31 is acceptable for use.

Review:

The following comments were sent to Instituto Biolon on the lot release protocol template submitted on 9/12/2013 in the supplement 125488/0.23:

1. In the header the top line should read: cc: 125488_0/1900/ -FC
2. In the Stabilizer section of page 1, please correct the spelling of "Glicyne" to "Glycine".
3. On page 2 the growth promotion test information is not required in the sterility template. Also on page 2 in the sterility template, please add the following after the table with the data:

Result:

Specification:

See example:

Sterility

Method used: _____

Type: for example, Viral Harvests, Bulk, Final Container

B&F Test Date:

| On Test Date | Medium/Temperature | Tested Quantity | Off Test Date |
|--------------|--------------------|-----------------|---------------|
| | | | |
| | | | |

Result:

Specification:

- 4. When submitting a completed lot release protocol, please include the date of the B&F test performed to confirm the product matrix is suitable for the intended test method.
- 5. On page 3, please add a column for test dates and a column for the test result.
- 6. For the General Safety template on page 2, please include a section for Specification. An example has been provided below.

General Safety Test

Method used:

Specification:

| On Test Date | Animal Species | Route of Inoculation | Amount Inoculated | Weight (gm) | | Off Test Date |
|--------------|----------------|----------------------|-------------------|-------------|-------|---------------|
| | | | | Initial | Final | |
| | | | | | | |

Result:

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

If information contained in the lot release protocol changes please include an updated version of the lot release protocol template when submitting documentation for the changes.

Bioclon responded in amendment 125488/0.31 received 25-Nov-2013 with a revised lot release protocol template.

CBER had the following comments on the protocol received in amendment 125488/0.31; these were sent to Instituto Bioclon on 10-Jan-2014:

**1. On page 1, just a reminder, that for regular lot release the line in front of For Release should be marked. Example: X For Release
Also on page 1, the line “STN: BL-125488/0” should be removed and only used for samples being submitted to the original BLA or when associated with a supplement, and the supplement number would replace the 0. Example 125488/four digit assigned number.**

Instituto Bioclon Response:

Instituto Bioclon confirms that for regular lot release the line in front of ‘For Release’ will be marked.

Instituto Bioclon confirms that line “STN: BL-125488/0” will be removed and only used for samples being submitted to the original BLA or when associated with a supplement, and the supplement number would then replace the 0.

2. On page 2, for the Rabbit Pyrogen test, the dose is 5 mL, this should be based on the weight (kg) of the rabbit so it is unlikely they would all be exactly the same. Please confirm that the dose will be adjusted based on the weight of the rabbit. The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Instituto Bioclon Response:

Instituto Bioclon confirms that the dose will be adjusted based on the weight of the rabbit.

If a supplement is submitted that impacts the lot release protocol, please submit an updated lot release protocol with the supplement. This includes changes to specifications or the addition of a test.

CBER response: These responses are acceptable.