



MEMORANDUM

From: Varsha Garnepudi
Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To: **Biologics License Application Submission Tracking Numbers # 125613**

Subject: **Review of Lot Release Protocol Templates of Biologics License Application for KEDRAB** (Rabies Immune Globulin (Human)).

Through: Lokesh Bhattacharyya, Acting Director, DBSQC/OCBQ/CBER/FDA

Cc: Qian Jiahua, RPM
Michael Kennedy, Chair, BLA Review Committee

Applicant: Kamada Ltd.

Products: **KEDRAB**

1 General Information

1.1 CMC Review Identifiers and Dates

1.1.1 Biologics License Application (BLA) Submission Tracking Numbers (STN) #: 125613

1.1.2 Submissions received by CBER: August 29, 2016

1.1.3 Review completed: August 16, 2017

1.1.4 Material Reviewed:

Original BLA: The following general module sections of the BLA were reviewed: M3 CMC, Quality

2 Review

2.1 Documents Reviewed

1. Draft Lot Release Protocol Templates submitted in amendment
 - a. 125613/0.0 on 08 August, 2016
 - b. 125613/0.18 on 06 April, 2017
 - c. 125613/0.31 on 04 August, 2017
 - d. 125613/0.32 on 15 August, 2017

2.2 Review

The submission is an original BLA submitted by Kamada to obtain licensure for Rabies Immune Globulin (Human).

The LRP template submitted in the 125613/0 was reviewed by DPPT and DBSQC with comments. The following Information Request was sent on 31st March, 2017 to continue our review.

- a. On Page 5 of 5 please change the Sterility specification from (b) (4) [REDACTED].
- b. On page 4 of 5 (Table: (b) (4) [REDACTED]) and page 5 of 5 pages (Table: Final Container Test) please include two columns - one for test method reference / SOP number and the second for test date.

- c. On page 5, (b) (4) Test, please explain how this is different from (b) (4) test mentioned on page 4 under (b) (4).

A response to the 31st March, 2017 information request was received in an amendment 125613/0.18, on 6th April, 2017.

Kamada responses for items (a-b).

The Lot Release Protocol Template was amended per FDA's request.

Kamada response for item c.

Kamada confirms that there is no difference between the two tests.

CBER Response: Kamada has addressed all CBER comments adequately.

The following Information request was sent on 1st August, 2017 by CMC reviewers from DPPT.

1. Please change the specifications of "Visible Particles" for (b) (4) DP to "May contain some protein particles".
2. Please note that there is a typographic error in "Clarity and Degree of Opalescence" specification for (b) (4) DP. Please change the specification to "The solution is clear to slightly opalescent."
3. Regarding the Protein Identity test:
 - a. Please confirm that the test is performed after product packaging and include this information into Section 2.2 under 3.2.P.5.2 Analytical Procedures section and the SOP N-IP-5344-17.
 - b. Please clarify how your Protein Identity test distinguishes KEDRAB from all other products manufactured by Kamada. If the assay is not specific to KEDRAB, please implement a specific assay.
4. Please update ALL the documents accordingly including Lot Release Protocol Template and product release and stability specifications for DS and DP.

A response to the 1st August, 2017 information request was received in an amendment 125613/0.31 on 4th August, 2017.

Kamada responses for Items (1-4).

- The Lot Release Protocol was updated for the Specification for "Visible Particles" for (b) (4) DP to state "May contain some protein particles".

- The typographic error in “Clarity and Degree of Opalescence” specification for (b) (4) DP was corrected to state “The solution is clear to slightly opalescent”.
- Kamada has revised the identity testing for release to include Protein Identity as well as Identification by (b) (4) ; The Lot Release Protocol was updated to include the Protein Identity and the Identification by (b) (4) test.
- The Lot Release Protocol was updated in response to the August 1, 2017 information request in amendment 125613/0.31 and 125613/0.32 received on August 4th and 15th, 2017.

CBER Response: Kamada has addressed all CBER comments adequately.

During a conference call meeting with Kamada on 9th August, 2017, Kamada committed to develop and validate an adequate method for (b) (4) analysis and add a specification for (b) (4). This will be addressed via a post marketing commitment (PMC). It will be necessary to revise the LRP to add the specification and test results for (b) (4) after the PMC is completed and approved.

2.3 Conclusions

Final Lot release protocol templates submitted, as listed in section 2 for this STN in 125613/0.32 is acceptable for use. Following completion of post marketing commitment the specifications for the (b) (4) will be updated in the LRP template.