DEPARTMENT OF HEALTH & HUMAN SERVICES

Division of Biological Standards & Quality Control, Office of Compliance & Biologics Quality,
Center for Biologics Evaluation & Research, Food & Drug Administration

MEMORANDUM

From Alfred Del Grosso, Ph.D., LACBRP/DBSQC/OCBQ

Mark Levi, Ph.D., LACBRP/DBSQC/OCBQ

To STN 125549/0

Through Lokesh Bhattacharyya, Ph.D., Chief, LACBRP, OCBQ/DBSQC

William M. McCormick, Ph.D., Director, OCBQ/DBSQC

Sponsor Pfizer Inc.

Product Meningococcal Group B Vaccine (Trumenba)

Subject DBSQC Review Memo for Chemistry Related Test Methods

Review Summary and Recommendation

Specific Assays Reviewed and addressed in this memo include:

1) Aluminum (DP)
2) PS 80 ----------(b)(4)---------- DP)
3) ----------(b)(4)----------
4) -----(b)(4)----- (DP)
5) Appearance (DP)
6) pH ((b)(4) DP)
7) Volume of Injection (DP)

Procedures and Validations, including the responses by Pfizer to CBER Information Requests and proposed Post Marketing Commitments have been reviewed and evaluated as adequate for their intended purposes.

Review Narratives

1. **Aluminum Content by ---(b)(4)--- (Drug Product)**

   Primary Reviewer: Mark Levi

   Documents reviewed

3.2.P.5.2: "Aluminum Test Method"
3.2.P.5.3 Method Validation Report - Aluminum Validation
SOP-13511 – Determination of Aluminum content in MnB rLP2086 Drug Product by ---(b)(4)---

Method

Aluminum is present in the MnB drug product at ----------(b)(4)----------. A summary of the method was included in the BLA submission. Pfizer's SOP was submitted in Amendment 21 as part of a response to a CBER Information Request.

This method is used as a quantitative assay for measurement of the aluminum (Al) concentration in samples containing aluminum phosphate as a ----(b)(4)---- of the rLP2086 proteins. ----------(b)(4)----------.

Method Validation

The following characteristics were studied to validate the method: Specificity, Linearity, Precision (Repeatability and Intermediate Precision), Accuracy, and Range. This is a quantitative method.

Repeatability was determined by analyzing (b)(4) preparations of drug product. The mean Al concentration was ---(b)(4)--- with a %RSD value of (b)(4), meeting the requirement of (b)(4).

Intermediate Precision was determined by analyzing (b)(4) preparations of drug product on -------(b)(4)--------. Mean Al value was ---(b)(4)--- with a %RSD value of (b)(4), meeting the requirement of (b)(4).

Specificity for Al was examined by analyzing ----------(b)(4)----------. The requirement was met that the difference should be (b)(4).

Linearity of the standard was determined using ----------(b)(4)----------

----------(b)(4)---------- values met the acceptance criteria of -(b)(4)-

Accuracy was determined by ----------(b)(4)----------. Values obtained with ---(b)(4)--- were within specifications of ---(b)(4)--- for recovery and (b)(4) RSD.

Range of the assay was determined from the accuracy test above. The range of the assay was established from ----(b)(4)----. This is reasonable.

Information Request: A CBER information request related to the Aluminum procedure was made on August 29, 2014. A summary of the procedure had been submitted with the original quality amendment 125549/0.2 Section 3.2.P.5.2. This was evaluated as lacking sufficient detail to allow a complete review. Additionally minor inadequacies were noted in the validation summary Section 3.2.P.5.3 concerning the evaluation of linearity. A response by Pfizer was received on 9/24/14. CBER's requests and the responses are as follows:

Question 27.

a. Please provide a fully descriptive procedure.

   Response: Pfizer is submitting the detailed procedure in the form of the current SOP (SOP-13511 Determination of Aluminum in MnB rLP2086 Drug Product by ---(b)(4)---) for the aluminum determination of drug product with this response.

b. In Section 3.2.P.5.2.3.1 (Standard Curve Preparation), it states that "Typically (b)(4) concentrations ranging from approximately ---(b)(4)--- are prepared." Please specify the actual concentration range to be used in practice of the assay. Please revise your procedure to use (b)(4) concentration points.

   Response: In the current method, Pfizer uses ----------(b)(4)---------- calibration standards. Pfizer will update the method for aluminum determination of drug product to include (b)(4) concentration points within the validated range of the assay. In addition, Pfizer will provide an assessment of linearity of the --(b)(4)-- standard curve. As this will require additional work, Pfizer respectfully requests that this change be a post-marketing commitment and will provide the revised method and any relevant validation data by September 30, 2015. Given that the revised calibration curve will also be within the validated range of the assay, it is not anticipated that there would be any significant change to results generated to date with this assay. The updated method will be applied to assess the aluminum concentration of batches produced after implementation of the post-marketing commitment.

c. In Section 3.2.P.5.2.3.3 (Sample Preparation), it states that samples are

-------(b)(4)------- for an appropriate time (e.g. -(b)(4)-). Please specify the time to which samples of the MnB rLP2086 Drug Product are to be -(b)(4)- or what other criteria is used to determine the time of --(b)(4)--.

Response: According to the method for aluminum determination, the MnB rLP2086 drug product samples are ---(b)(4)--- for a minimum of (b)(4) before analysis.

d. The Validation report summary for Aluminum (Section 2.5.11, Experimental Design) describes the evaluation of linearity based on (b)(4) concentration levels ---(b)(4)--- prepared once and injected once. Please submit an evaluation of linearity using at least (b)(4) concentrations levels to cover the intended range of the assay procedure.

Response: As stated above in the response to question 27 (b), Pfizer will update the method for aluminum determination of drug product to include (b)(4) concentration points. In addition, Pfizer will provide an assessment of linearity of the (b)(4) standard curve. As this will require additional work, Pfizer requests that this change be a post-marketing commitment and will provide the revised method and any relevant validation data by September 30, 2015. As we intend to stay within the validated range of the assay, there should be minimal impact on the results generated to date with this method. The updated method will be applied to assess the aluminum concentration of batches produced after implementation of the postmarketing commitment.

Conclusion

The method is generally acceptable on an interim basis for the intended use as a component assay in the drug product. The commitment by the sponsor to provide a revised method and validation data by Sept.30, 2015 to include five concentration levels of standards is acknowledged.

2. Polysorbate 80 ----------(b)(4)---------- DP)

Primary Reviewer: A. Del Grosso

Documents reviewed

3.2.S.4.2 Polysorbate 80 ---------(b)(4)----------

3.2.S.4.3 Summary Report for Validation of the Polysorbate ------(b)(4)---------

Method for MNB RLP2086 ------(b)(4)-------

3.2.P.5.2 Polysorbate 80 --------(b)(4)---------- (DP)

3.2.P.5.3 Summary Report for Validation of Polysorbate 80 --------(b)(4)----------

Method for MNB Bivalent RLP2086 Drug Product

Method

---(b)(4)---
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2 pages redacted (b)(4)

3. ----------**(b)(4)**----------

Primary Reviewer: A. Del Grosso

Materials Reviewed
3.2.S.4.3 Analytical Procedures – ----------(b)(4)----------
3.2.S.4.3 Validation of Analytical Procedures – ----------(b)(4)----------
3.2.P.5.2 Analytical Procedures – ----------(b)(4)----------
3.2.P.5.3 Validation of Analytical Procedures – ----------(b)(4)----------
125549/0.21 – SOP 13655 Determination of ----------(b)(4)--------- in MnB rLP2086 Drug Product Samples by ----(b)(4)---

Method

----------(b)(4)----------.

----------(b)(4)----------.

----------(b)(4)----------.

----------(b)(4)----------.

----------(b)(4)----------.

----(b)(4)----

3 pages redacted (b)(4)

4. ---(b)(4)--- Primary Reviewer: A. Del Grosso

---(b)(4)--- is determined using a method consistent with ----------(b)(4)----------.
Drug product specification ----------(b)(4)----------.

Conclusion: Acceptable.

5. pH Primary Reviewer: A. Del Grosso

pH is determined using a method consistent with ----------(b)(4)----------.
Drug product specification is pH 6.0 (b)(4).

Conclusion: Acceptable.

6. Appearance Primary Reviewer: A. Del Grosso

Appearance is determined by a visual method. As described, drug product syringes are ----------(b)(4)---------- and inspected in their original containers. Samples are mixed well by vigorous shaking until homogeneous. Color is recorded and samples are assessed for clumps or aggregation. Specification is "Homogeneous white suspension".

Conclusion: Acceptable.

7. Volume of Injection Primary Reviewer: A. Del Grosso

Volume of Injection is determined by a ----------(b)(4)----------. Specification is (b)(4) 0.5 mL.

Conclusion: Acceptable.