Center for Biologics Evaluation and Research
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DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file STN 125748/0

From:

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Hsiaoling Wang	Lead Reviewer	05/04/2022		Tao Pan	
Claire H. Wernly	Reviewer	03/11/2022		James Kenney	
Noel Baichoo	Reviewer	05/11/2022		Muhammad Shahabuddin	

Through: Maryna Eichelberger, Ph.D.
Division Director, DBSQC/OCBQ

Applicant: GlaxoSmithKline Biologicals (GSK)

Subject: Review of Analytical Methods used for Priorix Drug Substances (DSs) and Drug Product (DP) Lot Release

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Recommendation: Approval

Executive Summary:

The following analytical methods used for lot release of Priorix and the associated analytic method validations or qualifications, were reviewed:

1. Determination of Water Content of Drug Product by (b) (4) (Hsiaoling Wang)
2. Appearance and (b) (4) of Drug Product (Hsiaoling Wang)
3. Tests for Drug Product Diluent: Appearance, (b) (4) (Hsiaoling Wang)
4. Sterility Test of (b) (4) Drug Product (Claire H. Wernly)
5. (b) (4) Test of (b) (4) (Claire H. Wernly)
6. Identity of MRC-5 cells for rubella production (Noel Baichoo)
7. Identity of (b) (4) Drug Product components (Noel Baichoo)
8. Potency of (b) (4) Drug Product components (Noel Baichoo)

Conclusion: The analytical methods and their validations and qualifications reviewed for Priorix drug substances and drug product were found to be adequate for their intended use.

Documents Reviewed

Information in sections of the original submission that describe controls of DS and DP (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and validation of these analytical procedures were reviewed. Additional information in amendments specified by each reviewer were also reviewed.

Background

GSK submitted an original Biologics License Application (BLA), STN 125748, on June 4, 2021, for Priorix, a live attenuated viral vaccine for active immunization for the prevention of measles, mumps, and rubella in individuals aged 12 months and older through subcutaneous injection. The Priorix DSs are bulks of the Schwarz strain of live attenuated measles virus, the RIT 4385 strain of live attenuated mumps and the Wistar RA 27/3 strain of live attenuated rubella virus, which are clarified viral suspensions and stored at (b) (4). The Measles and the Rubella monovalent bulks are both stabilized in a solution containing sorbitol, amino acids and inorganic salts. The mumps monovalent bulk is stabilized in a solution containing sorbitol, lactose, amino acids and inorganic salts.

The Priorix DP consists of two components, both are stored at 2-8°C before use: 1) Lyophilized powder containing the Measles (M), Mumps (M) and Rubella (R) antigens in a mono-dose vial; 2) Water for Injection (WFI) diluent provided in a mono-dose prefilled syringe. Priorix is reconstituted only with the accompanying sterile WFI diluent before administration. Each dose is approximately 0.5 mL. The first dose of Priorix is administrated subcutaneously at 12 to 15 months of age and the second dose at 4 to 6 years of age.

The following facilities perform the methods reviewed:

- (b) (4): Release testing of the Measles, Mumps and Rubella monovalent bulks (DS); Release testing of Final Bulk and Final Container (DP)
- (b) (4): MMR vaccine visual inspection; Release testing of MMR Final Bulk, Final Container and Final Product (DP); Release testing of WFI diluent Final Product (DP)
- (b) (4) WFI Diluent release testing (DP)
- (b) (4): Release of Mumps monovalent bulk (DS)

1. Determination of Water Content by (b) (4)

The water content specification for lyophilized Priorix powder in final container is not more than (b) (4)

Method

The water content in the lyophilized cake is determined by the (b) (4)

The water content in a sample is determined by (b) (4)

(b) (4)

(b) (4)

(b) (4)

1 page determined to be not releasable: (b)(4)

(b) (4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and the amendments, the method has been validated for its intended purpose.

2. Appearance (b) (4) of DP final container

Appearance

The specification of the lyophilized DP component is whitish to slightly pink colored cake or powder. After reconstitution with the diluent, it is clear peach to fuchsia pink colored solution.

Method

The analytical procedure is described in SOP No. 9000007041. The samples are visually inspected and examined in their initial containers in a light inspection station against (b) (4)

(b) (4)

If foreign matter is present in a sample, report the observation including color, shape, or other relevant properties of the foreign matter for further investigation while the presence of fine white particles is acceptable.

An IR was sent to the firm on Sep. 12, 2021, regarding the quality of (b) (4) used for color comparison. The firm responded in amendment 7 on Oct. 5, 2021 that the (b) (4) is printed (b) (4) The response is satisfactory.

(b) (4)

(b) (4)

3. Tests for DP Diluent

Appearance

The specification of DP diluent is clear, colorless and free from visible particles.

Method

The analytical procedure is described in SOP No. 9000007113. A minimum of (b) (4) DP diluent syringes are tested for appearance. (b) (4)

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(b) (4)

(b) (4)

Conclusion

Based on the information provided in the original BLA and the amendment, these three compendial methods have been verified for their intended purposes.

4. Sterility Test for (b) (4) Drug Product

This test is performed on the (b) (4) for Measles, Mumps and Rubella as well as the combined, final container (i.e., Measles–Mumps-Rubella [MMR] vaccine) and the lyophilized MMR drug product at the (b) (4) site.

Method

GSK performs sterility testing using the (b) (4)

(b) (4)

(b) (4)

An IR was sent to the firm on November 15, 2021, requesting qualification report for sterility test. The firm responded in amendment 15 on December 10, 2021. After additional review, all requested information was found in the original submission.

Conclusion

After a thorough review of the BLA, this reviewer finds the sterility test method was qualified in accordance with (b) (4) and demonstrated to be suitable under the actual conditions of use. Therefore, this reviewer finds this method acceptable for its intended purpose and recommends its approval.

(b) (4)

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(b) (4)

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7. Identity of (b) (4) Drug Product Components

Two identity methods are described; in one (SOP 9000061338), the identity of measles, mumps, and rubella viruses in manufacturing (b) (4) DP is determined by (b) (4) at the (b) (4) site. In the second (SOP 9000063875), (b) (4) is also used but this assay is limited to testing for measles and varicella viruses in the packaged final product at the (b) (4) site in (b) (4) .

Method 1

(b) (4)

Method 1 validation

(b) (4)

(b) (4)

Method 2

(b) (4)

(b) (4)
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Method 2 validation

(b) (4)

Conclusion

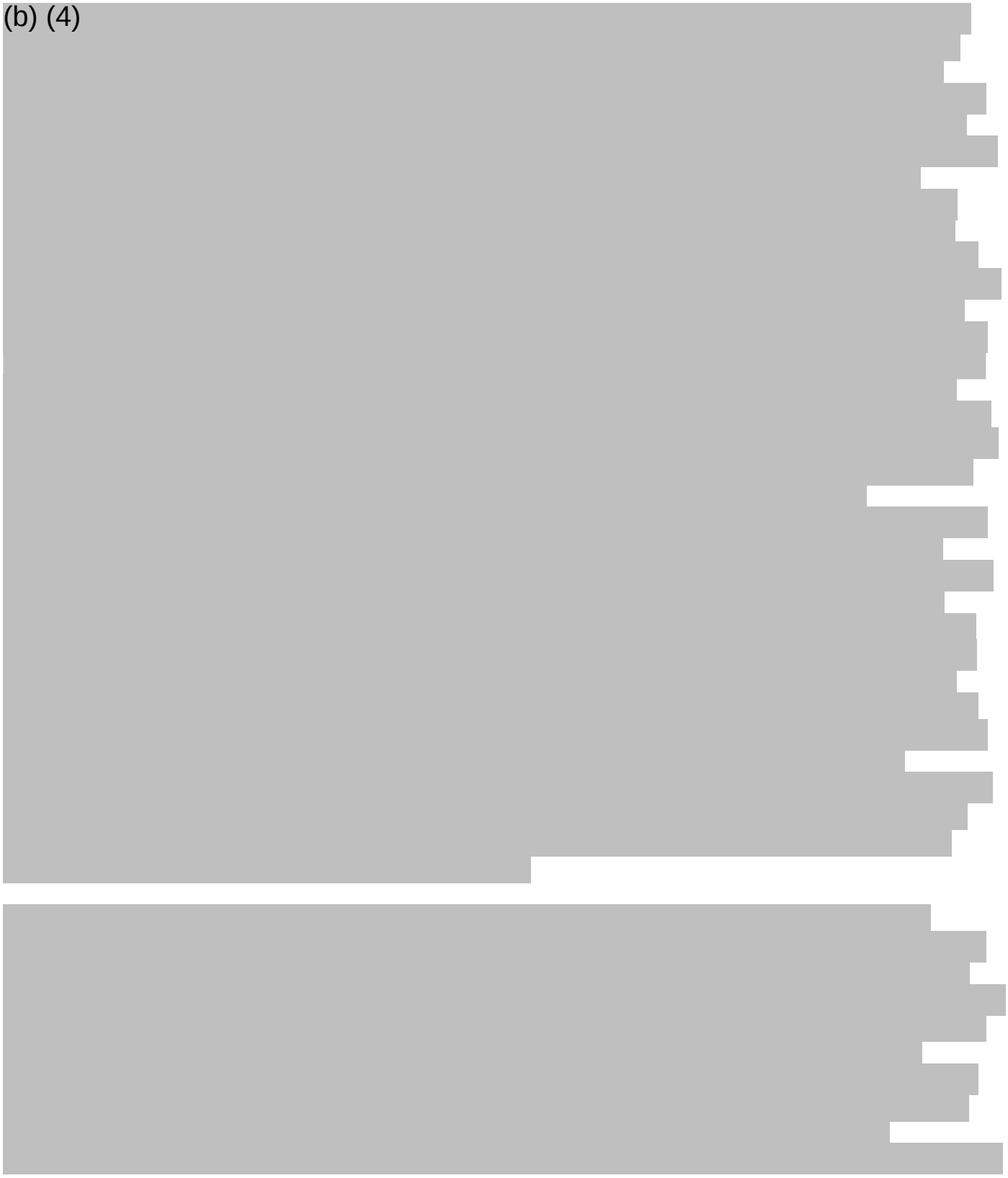
The identity assays for measles, mumps, rubella and the absence of varicella are adequately described and are appropriate for release of (b) (4) DP.

8. Potency of (b) (4) Drug Product Components

The (b) (4) of each infectious vaccine component (measles, mumps, and rubella viruses) is used as the measure of potency. The (b) (4) of measles and mumps are both measured on (b) (4) and therefore are described in a single procedure, while rubella potency is measured on (b) (4) . The assays are performed at (b) (4) for lot release of (b) (4) DP.

Method 1: Measles and mumps potency assay

(b) (4)



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(b) (4)

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Method 2: Rubella potency assay

(b) (4)

[redacted]

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(b) (4)

[redacted]

Conclusion

The assays used to determine measles, mumps and rubella potencies are well described and validated. They are suitable for lot release testing of (b) (4) DP.