

DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file STN 125775/0

From:

Reviewer	Role	Date finalized	Stamp	Supervisor	Stamp
Jing Lin, Ph.D.	Lead Reviewer	4/28/2023		Muhammad Shahabuddin, Ph.D.	
Simleen Kaur, M.S.	Reviewer	3/20/2023		James L. Kenney, D.Sc.	
Hsiaoling Wang, Ph.D.	Reviewer	4/24/2023		Kenneth Phillips, Ph.D.	
Ritu Agarwal, Ph.D.	Reviewer	4/30/2023		Kenneth Phillips, Ph.D.	

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

Applicant: GlaxoSmithKline Biologicals

Subject: Review of Analytical Methods used for Respiratory Syncytial Virus Vaccine, Adjuvanted (b) (4) Drug Product (DP) Lot Release

Recommendation: Approval

Executive Summary:

The following analytical procedures and associated method validations or qualifications for Respiratory Syncytial Virus Vaccine Recombinant, Adjuvanted (AREXVY) were reviewed:

1. RSVPreF3 Identity and In Vitro Relative Potency (b) (4) (Jing Lin)
2. (b) (4) (Jing Lin)
3. (b) (4) (Jing Lin)
4. Sterility Test on DP (Simleen Kaur)
5. Endotoxin Test on (b) (4) DP (Simleen Kaur)
6. (b) (4) (Simleen Kaur)
7. RSVPreF3 (b) (4) DP (Hsiaoling Wang)
8. (b) (4) AS01E (Adjuvant) (DP) (Hsiaoling Wang)

9. MPL (b) (4) AS01_E (Adjuvant) (DP) (Hsiaoling Wang)
10. (b) (4) AS01_E (Adjuvant) DP and RSVPreF3 DP (Hsiaoling Wang)
11. (b) (4) RSVPreF3 DP (Hsiaoling Wang)
12. Polysorbate 80 Content (b) (4) RSVPreF3 DP (Hsiaoling Wang)
13. Determination of trehalose content in RSVPreF3 DP samples (b) (4) (Hsiaoling Wang)
14. RSVPreF3 (b) (4) (Ritu Agarwal)
15. Tests performed on AS01_E Adjuvant (Ritu Agarwal)
 - a) Cholesterol and DOPC content (b) (4)
 - b) DOPC content (b) (4)
 - c) QS-21 (b) (4)
 - d) (b) (4)
 - e) (b) (4)
16. Appearance (appearance, color, opalescence) (Ritu Agarwal)
17. (b) (4) (Ritu Agarwal)

Conclusion: The analytical methods and their associated method validations reviewed for Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY) were found to be adequate for their intended use.

Documents Reviewed:

Information in sections of the original BLA (STN125775) submissions that describe control of (b) (4) DP and AS01_E adjuvant (3.2.S.4 and 3.2.P.5), including descriptions of (b) (4) DP and AS01_E specifications, analytical procedures of (b) (4) DP and AS01_E as well as validation of these analytical procedures were reviewed. Additional information in amendments that are listed in the narrative below were also reviewed.


Background:

On September 2, 2022, GlaxoSmithKline Biologicals SA (GSK) submitted an original BLA, STN 125775/0, for AREXVY, a recombinant adjuvanted Respiratory Syncytial Virus (RSV) Vaccine indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by RSV-A and RSV-B subtypes in adults 60 years of age and older.

RSV, a member of the Paramyxoviridae family of nonsegmented, negative-sense, single-stranded RNA genome viruses, is a leading cause of lower respiratory tract infections in infants, young children, and the elderly or immunocompromised. RSV is classified into two subtypes, A and B, whose predominance alternates during different epidemic seasons.

The RSV F protein was selected as vaccine antigen due to being a major surface antigen of the RSV virus that is well conserved among RSV-A and RSV-B subtypes. (b) (4)

(b) (4)





This engineered version of RSV fusion (F) protein is named RSVPreF3.

AREXVY is supplied as single-dose vials of lyophilized RSVPreF3 antigen (and excipients) to be reconstituted with the accompanying vial of adjuvant suspension, AS01E, a variant of the AS01 family. One dose AS01E contains 25 µg of each of the immunoenhancers Quillaja saponin-21(QS-21) and monophosphoryl lipid A (MPL) using liposomes (consisting of dioleoyl phosphatidylcholine and cholesterol) as a vehicle. After reconstitution, a single dose of 0.5 mL contains 120 µg of RSVPreF3 antigen adjuvanted with AS01E.

Review:

1. RSVPreF3 Identity and In Vitro Relative Potency (b) (4) (Jing Lin)

(b) (4)

4 Pages have been determined to be not releasable:(b)(4)

(b) (4)


II. Drug Product

Method validation for the lyophilized Drug Product (RSVPre3 Lyo) was documented in Analytical Method Validation Report: 9000068071 RVM002_001 V1- Method Validation of “RSV PreF3 Identity and In Vitro Relative Potency” (b) (4) for RSV Containing Vaccine on Drug Product. The same validation parameters as used for testing (b) (4) were evaluated. DP (b) (4) were used as samples.

(b) (4)

13 Pages have been determined to be not releasable: (b)(4)

(b) (4)




4. Sterility Method (Simleen Kaur)

Introduction

Sterility testing is performed on the DP at GSK's (b) (4) facility in Belgium only. The test on AS01_E adjuvant is performed at (b) (4) facility in Belgium (b) (4). Acceptance criteria of 'No Growth Detected' must be met for the lot release of AREXVY DP and AS01_E adjuvant.





Method

(b) (4)




34 Pages have been determined to be not releasable: (b)(4)


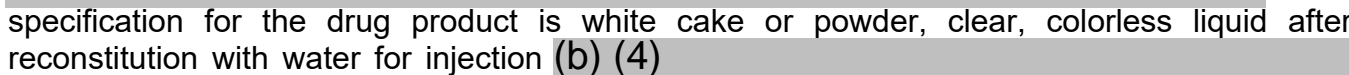
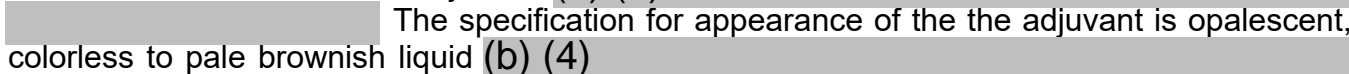
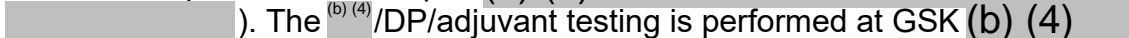
(b) (4)



(b) (4)



16. Appearance (Ritu Agarwal)

The specification for appearance of the (b) (4) . The specification for the drug product is white cake or powder, clear, colorless liquid after reconstitution with water for injection (b) (4) . The specification for appearance of the the adjuvant is opalescent, colorless to pale brownish liquid (b) (4) ). The ^{(b) (4)}/DP/adjuvant testing is performed at GSK (b) (4) , Belgium.

Method

Appearance

The characteristic of finished product in final container is examined visually (b) (4)
(as per the method described in SOP-9000031207).

(b) (4)