

CBER DMPQ CMC/Facility BLA Review Memorandum

BLA STN 125775

AREXVY (Respiratory Syncytial Virus Vaccine, Adjuvanted)

Erin Hill, CMC/Facilities reviewer, CBER/OCBQ/DMPQ/MRB2

1. BLA#: STN 125775

2. APPLICANT NAME AND LICENSE NUMBER

GlaxoSmithKline Biologicals SA, License # 1617

3. PRODUCT NAME/PRODUCT TYPE

Non-Proprietary/Proper/USAN: Respiratory Syncytial Virus Vaccine, Adjuvanted

Proprietary Name: AREXVY

4. GENERAL DESCRIPTION OF THE FINAL PRODUCT

- a. Pharmacological category: Recombinant vaccine
- b. Dosage form: Suspension for injection
- c. Strength/Potency: A single dose of 0.5 mL contains 120 mcg of RSVPreF3 antigen adjuvanted with AS01E
- d. Route of administration: Intramuscular injection
- e. Indication(s): Indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus RSV-A and RSV-B subtypes in adults 60 years of age and older.

5. MAJOR MILESTONES

Application Received: September 2, 2022

Filing Meeting: October 17, 2022

First Action Due: May 3, 2023

6. DMPQ CMC/FACILITY REVIEW TEAM

Reviewer/Affiliation	Section/Subject Matter
Erin Hill, Consumer Safety Officer (CSO), CBER/OCBQ/DMPQ/MRB2	3. Quality 3.2.S Drug Substance 3.2.P Drug Product (Antigen) 3.2.P Drug Product (Adjuvant) 3.2.A.1 Facilities and Equipment

7. SUBMISSION(S) REVIEWED

Date Received	Submission	Comments/ Status
September 2, 2022	STN 125775/0	Original Submission
November 4, 2022	STN 125775/0.4	Response to IR on October 21, 2022

Date Received	Submission	Comments/ Status
September 2, 2022	STN 125775/0	Original Submission
February 10, 2023	STN 125775/0.17	Response to IR on February 3, 2023
March 20, 2023	STN 125775/0.27	Response to IR on March 13, 2023
March 23, 2023	STN 125775/0.28	Response to IR on March 16, 2023
March 24, 2023	STN 125775/0.29	Response to IR on March 22, 2023
April 7, 2023	STN125775/0.36	Response to IR on April 4, 2023

8. REVIEWER SUMMARY AND RECOMMENDATION

A. EXECUTIVE SUMMARY

GlaxoSmithKline Biologicals SA (GSK) submitted a Biologics License Application (BLA) on September 2, 2020, under STN125775/0 for the licensure of the AREXVY (Respiratory Syncytial Virus Vaccine, Adjuvanted), hereafter referred to as AREXVY, for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus RSV-A and RSV-B subtypes in adults 60 years of age and older. This DMPQ review memo includes summaries and assessments of the drug substance (DS) and drug product (DP) manufacturing process, microbial quality attributes, facility information including utilities, cross-contamination controls, qualification and maintenance of classified environments and manufacturing equipment, and cleaning and sterilization processes.

The pre-license inspections (PLI) for the (b) (4) DP (b) (4) Belgium (b) (4) facilities) manufacturing facilities and the final release testing facility (b) (4) are waived based on their inspection histories and compliance status. The basis for waiving the inspection of these facilities is documented in a separate inspection waiver memo dated March 8, 2023.

Based on the information submitted to BLA 125775/0 and in conjunction with the inspectional compliance history evaluations, the product manufacturing process, facilities, equipment, and controls appear acceptable for the licensure of AREXVY; approval is recommended.

B. RECOMMENDATION

I. APPROVAL

Based on the information provided in the submission, approval is recommended with inspectional recommendations. CBER understands that the recommendation may or may not be taken (based on risk and available resources) and is not requesting documentation to be submitted as evidence of completion.

GlaxoSmithKline SA in (b) (4) Belgium, FEI#: (b) (4)

(b) (4)

II. SIGNATURE BLOCK

Reviewer/Title/Affiliation	Concurrence	Signature and Date
Erin Hill, CSO, CBER/OCBQ/DMPQ/MRB2	Concur	
Anthony Lorenzo, Branch Chief, CBER/OCBQ/DMPQ/MRB2	Concur	
Carolyn Renshaw, Director, CBER/OCBQ/DMPQ	Concur	





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Module 3


3.2.S DRUG SUBSTANCE




(b) (4)





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

(b) (4)



3.2.P DRUG PRODUCT (RSVPreF3)


3.2.P.1 Description and Composition of the Drug Product

The RSVPreF3/AS01E vaccine is a sterile, adjuvanted, preservative-free liquid suspension and consists of two components, each provided as a monodose preparation: a white powder (lyophilized preparation) containing the RSV recombinant fusion protein RSVPreF3 and a liquid suspension consisting of the AS01E Adjuvant System. The Adjuvant System is used to reconstitute the RSVPreF3 lyophilized antigen immediately prior to administration.

RSVPreF3 lyo container closure system is a one-dose vial presentation and includes a 3 mL Type (b) (4) glass vial with a 13 mm bromobutyl rubber stopper and aluminum cap.

3.2.P.2.5 Microbiological Attributes

The RSVPreF3 DP is sterile and is manufactured with (b) (4), phosphate buffer, trehalose, and polysorbate 80 that have all been (b) (4)



finished DP is tested for sterility and endotoxin prior to release. The CCS components are received sterile and RTU, and incoming lots of CCS components

are tested for sterility. The container closure system was evaluated by testing for compatibility, protection from light in the opaque secondary packaging, container closure integrity testing (CCIT), and performance. Refer to 3.2.P.7 for the CCIT.

3.2.P.3 Manufacture

3.2.P.3.1 Manufacturer(s)

See section 3.2.A.1 for a complete list of DP manufacturers.

3.2.P.3.3 Description of Manufacturing Process

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

(b) (4)

Lyophilization

The lyophilization process consists of (b) (4)

Labeling and Packaging

Primary labeling of the vials, and secondary packaging with the adjuvant system occurs at the GSK (b) (4) facility (building (b) (4)), GSK (b) (4) facility (building (b) (4)), (b) (4) facility (building (b) (4)). Vials are labeled using on an automatic labeling machine with the lot number, expiration date, and other applicable information. The vials are placed inside of cartons with the product leaflet. The lot number, expiration date, and other applicable information is printed on each carton and the cartons are visually inspected and placed in grouping boxes. The boxes are placed on pallets and stored at 2-8°C until release.


Shipping of Final Drug Product

RSVPreF3 antigen and AS01E adjuvant system can be (b) (4) GSK facilities by means of (b) (4)

After labeling and packaging, the combined RSVPreF3 FC + AS01E final container finished product is stored at 2°C - 8°C.

(b) (4)

(b) (4)




Reviewer comment for section 3.2.P.3.3: *The description of the manufacturing process appears complete and sufficiently detailed. Refer to 3.2.P.3.4 Controls of Critical Steps and Intermediates, and 3.2.P.3.5 for controls associated with critical steps including operating and performance parameters, in-process controls, and hold-times. Diagrams of the shipping units and shipping configurations as well as (b) (4) to record temperature readings were reviewed appear acceptable.*


3.2.P.3.4 Controls of Critical Steps and Intermediates

Refer to section 3.2.P.7 *Container Closure System* for an assessment of CCIT.

(b) (4)



(b) (4)



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

(b) (4)

3.2.P.5 Control of Drug Product**3.2.P.5.1 and 3.2.P.5.6 Specification(s) and Justification of Specification(s)**

The release testing specifications for RSVPreF3 DP are provided in the following table. (b) (4) clinical, (b) (4) engineering, and (b) (4) PPQ RSVPreF3 final container lots were used to determine the acceptance criteria.

Table 20: RSVPreF3 Lyo Final Container Release Specifications

Test	Acceptance Criteria	Justification
Description	White cake or powder. Clear, colorless liquid after reconstitution with water for injection (b) (4)	Correspond to the visual inspection of the RSVPreF3 final container reconstituted with WFI
Endotoxin (b) (4)		
Sterility test (b) (4)	Absence of growth	Performed according to (b) (4) to confirm the sterility of the final container.
(b) (4)		

(b) (4)

Details of a sampling plan for quality release testing of final containers was provided in amendment STN 125775/0.27 (eCTD 0030) submitted March 13, 2023, at request of the OVRP reviewer. The sampling plan for tests within DMPQ purview are as follows:

(b) (4)

Reviewer comment for sections 3.2.P.5.1 and 3.2.P.5.6: DP specifications related to microbial control and sterility assurance appear acceptable. All other release specifications, associated justifications, and sampling plan data for RSVPreF3 lyo DP are deferred to the OVRP reviewers.

3.2.P.5.2 and 3.2.P.5.3 Analytical Procedures and Validation of Analytical Procedures

Refer to 3.2.P.7 for the assessment of CCIT.

The analytical procedures for testing for RSVPreF3 DP are provided in the following table.

Table 21: Analytical Procedures for Release Testing of the RSVPreF3 FC

Test	Reference
Description	In house analytical procedures
Endotoxin	Performed according to the (b) (4)
Sterility test (b) (4)	Performed according to (b) (4)
(b) (4)	21 CFR (Method of analysis 610.12 Sterility) (b) (4), to
(b) (4)	(b) (4)

Reviewer comment for sections 3.2.P.5.2 and 3.2.P.5.3: The firm is using a (b) (4) method for sterility testing by (b) (4). The assessment of all other analytical procedures for testing for RSVPreF3 lyo final container are deferred to the OVRP reviewers.

3.2.P.5.4 Batch Analyses

The table below details lots produced for PPQ-commercial that are followed in stability studies (process 2.4). The acceptance criteria for the PPQ-commercial lots are listed in Table 20 in section 3.2.P.5.1 and 3.2.P.5.6.

Table 22: RSVPreF3 Drug Product (b) (4) Final Container PPQ-Commercial Lots

(b) (4)

RSVPreF3 DP batch numbers are assigned sequentially. (b) (4)

Reviewer comment for section 3.2.P.5.4: (b) (4)

The PPQ lots were placed on stability studies. All available data was reviewed and discussed in section “3.2.P.8 Stability”. All results for batch analysis under DMPQ purview, are within the pre-defined QC release acceptance criteria. Review of the other tests performed are deferred to the OVRP reviewers.

3.2.P.7 Container Closure System

Vial containers, vial stoppers and vial flip-off caps are received separately and RTU, and assembly is carried out during the filling, lyophilization and packaging operations.

3 mL Vials

DP and the adjuvant are filled in 3 ml vial containers that are product contact Type (b) (4) uncolored glass that are manufactured by (b) (4)

Containers are sterilized by (b) (4)

acceptance criteria are listed in the table.

Table 23: 3 ml Vial Containers Acceptance Criteria

Test	Acceptance Criteria
(b) (4)	(b) (4)
Description	Type (b) (4) drawn uncolored glass vial
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
Visual control	Pass

The manufacturers and the representative certificates of analysis (CoA) for the Type (b) (4) 3 mL glass vial containers used for the RSVPreF3 formulated DP and AS01E adjuvant were provided in amendment STN 125775/0.27 (eCTD 0030).

13 mm Bulk Stoppers for Lyophilized Formulations

Stoppers are constructed of Bromobutyl type (b) (4) rubber and are received (b) (4) from the supplier, (b) (4). The stoppers are (b) (4) by GSK. They are product contact materials, (b) (4)

Table 24: 13 mm Bulk Vial Stoppers

Tests	Acceptance criteria
(b) (4)	(b) (4)
Description	In accordance with the reference sample
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
(b) (4)	(b) (4)
Visual control	Pass

Vial Flip-off Caps

Vial flip-off caps are used to secure the stopper to the vial and are constructed of a colored polypropylene top fixed on a natural aluminum varnished cap. The caps do not come into contact with the product and are not sterilized. (b) (4) manufactures the flip-off caps used for RSVPreF3 lyo CCS, (b) (4) manufactures the caps used for AS01E adjuvant system CCS.

Table 25: Vial Flip-off Caps

Tests	Acceptance Criteria
Aspect	<ul style="list-style-type: none"> Good appearance, neat and well finished Plastic disc is combined with the aluminum component to complete joining Polypropylene conforms to the particular specifications

Tests	Acceptance Criteria
(b) (4)	

The manufacturers and the representative CoA for the bulk stoppers and flip-off caps were provided in amendment STN 125775/0.36 (eCTD 0039).

Container Closure Integrity Test (CCIT)

CCIT was conducted using the (b) (4)

[REDACTED]

[REDACTED]

All results met the acceptance criteria, and no deviations were noted.

The number of vials tested per lot during the CCIT were provided in amendment STN 125775/0.36 (eCTD 0039).

Reviewer comment for section 3.2.P.7: OVRP sent an information request on March 13, 2023, requesting GSK to provide the manufacturers and the representative CoA for the Type (b) (4) 3 mL glass vial containers filled with RSVPreF3 formulated Drug Product. These deficiencies were addressed, and the data was provided in amendment STN 125775/0.27 (eCTD 0030) on March 20, 2023.

The RSVPreF3 lyo CCS materials of construction, critical dimensions, and generic schematic drawings for vial containers and vial stoppers for lyophilized formulations were reviewed and appear acceptable. The information provided regarding the CCIT appears acceptable.

3.2.P.8 Stability

3.2.P.8.1 Stability Summary and Conclusion and 3.2.P.8.3 Stability Data

GSK provided stability data for clinical, PPQ, and commercial lots. Stability data are generated for the RSVPreF3 final container DP and AS01E Adjuvant System lots, and the RSVPreF3/AS01E Reconstituted Vaccine (RV) lots. Refer to section 3.2.P.8.1 AS01E Adjuvant System, in this review memo for stability data regarding the adjuvant system. Stability data reviewed below covers PPQ and commercial lots. Lots (b) (4) were placed on long-term stability studies to support the storage of RSVPreF3 final container at 5°C ± 3°C for up to (b) (4) months. Lot (b) (4) was placed on a long-term stability study at 5°C ± 3°C for up to (b) (4) months to support the maximum RSVPreF3 final holding time. Samples were (b) (4), stored at 5°C ± 3°C, and description, sterility, and container closure tests were conducted. Only release data for all tests is available at this time.

Table 26: Stability Study Acceptance Criteria

Tests	Acceptance criteria	Time point (months)
Description	White cake or powder. Clear, colorless liquid after reconstitution with WFI	Release, 3, 6, 9, 12, 18, 24, (b) (4)
Sterility test (b) (4)	Absence of growth	Release, 6, 12, 24, (b) (4)
CCIT	(b) (4)	0, 24, (b) (4)

1. For the time points beyond claimed shelf-life no acceptance criterion is applied (record result).

Reviewer comment for sections 3.2.P.8.1 and 3.2.P.8.3: All available sterility, and CCIT results met acceptance criteria. Post-approval stability protocol for Phase 3 RSVPreF3 lyo lots and all other stability testing are deferred to the OVRP reviewers.

3.2.P DRUG PRODUCT (AS01E Adjuvant System)

3.2.P.1 Description and Composition of the Drug Product

AS01E Adjuvant System was developed by GSK and is the diluent used to reconstitute the RSVPreF3 vaccine. AS01E is a sterile, preservative-free liquid monodose vial preparation for intramuscular injection. The adjuvant system does not contain any (b) (4) and is composed of two immunoenhancers, QS-21 ((a triterpene glycoside purified from the bark of the tree *Quillaja saponaria* Molina) and MPL (3-Odesacyl-4'-monophosphoryl lipid A), additional excipients, and liposomes as a vehicle. The

pharmaceutical form of the Adjuvant System is an opalescent, colorless to pale brownish liquid suspension.

AS01E container closure system is a one-dose vial presentation and includes a 3 mL Type (b) (4) glass vial with a 13 mm chlorobutyl rubber stopper and aluminum cap.

3.2.P.2.5 Microbiological Attributes

The AS01 Adjuvant System is manufactured in a controlled environment to minimize bioburden and assure sterility of the final product. (b) (4)

(b) (4)

Filling and stoppering activities are automated and performed aseptically. AS01 Adjuvant System final container is tested for sterility. CCIT QD tests are performed on each final container batch. The control strategy in place for AS01E DP includes sterility, bioburden, and endotoxin testing:

- (b) (4)
- Endotoxin test (b) (4)

- Bioburden test:

- Sterility test: (b) (4)

3.2.P.3 Manufacture






3.2.P.3.1 Manufacturer(s)

See section 3.2.A.1 for a complete list of DP manufacturers.

3.2.P.3.3 Description of Manufacturing Process

The AS01E Adjuvant system is manufactured at the (b) (4), (b) (4) facility, and the facility located in (b) (4)

(b) (4)



Final containers are 100% visually inspected for fill volume, particles, and CCS conformity. A defined number of containers are sampled from each batch for QC release testing. Non-conforming containers are rejected, accounted for, and discarded. Inspected and approved containers are placed in boxes, palletized, and stored at 2-8 °C in the warehouse until labeling and packaging operations.

Labeling and Packaging

Primary labeling of the vials, and secondary packaging with the RSVPreF3 antigen occurs at the GSK (b) (4) facility (building (b) (4)), GSK (b) (4) facility (building (b) (4)) facility (building (b) (4)). The vials are labeled automatically on a labeling machine with a lot number, expiry date and other information. The vials are placed in a carton with leaflet and the lot number, expiry date and other information are printed on each carton. The cartons are visually check, placed in grouping boxes, palletized, and stored at 2°C - 8°C until release and shipping.

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

(b) (4)

- Finished product (b) (4) 2°C - 8°C:
 - RSVPreF3 and AS01E adjuvant system final product (b) (4)
 - RSVPreF3 and AS01E adjuvant system final product (b) (4)

GSK described how AS01E vials are packed (b) (4)
(b) (4) GSK facilities (b) (4) for labeling and packaging in
amendment STN 125775/0.25 (eCTD 0028) on March 8, 2023.

Reviewer comment for section 3.2.P.3.3: The manufacturing process appears acceptable. The information provided regarding the (b) (4) AS01E final containers appears to be acceptable.

3.2.P.3.4 Controls of Critical Steps and Intermediates

(b) (4)

(b) (4)

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

(b) (4)

3.2.P.5 Control of Drug Product**3.2.P.5.1 and 3.2.P.5.6 Specification(s) and Justification of Specification(s)**

The QC release specifications for AS01E Adjuvant System final container at the (b) (4) sites under DMPQ purview are listed in the table below.

Table 45: AS01E Final Container Release Specifications

Tests	Acceptance criteria	Justification
Sterility test (b) (4)	Absence of growth	Performed according to (b) (4) to confirm the sterility of the final container.

The acceptance criteria are based on the results obtained from (b) (4) AS01E development lots (b) (4) commercial (b) (4) final container lots. The acceptance criteria at release are the same as the acceptance criteria at the end of shelf life.

Reviewer comment for sections 3.2.P.5.1 and 3.2.P.5.6: The specifications related to sterility assurance appear acceptable. All other release specifications and associated justifications are deferred to the OVRP reviewers.

3.2.P.5.2 and 3.2.P.5.3 Analytical Procedures and Validation of Analytical Procedures

Refer to section 3.2.P.7 Container Closure System for assessment of CCIT.

3.2.P.5.4 Batch Analyses

QC release testing results for the RSVPref3 (b) (4) final container lots produced during development are listed below. All batches are used in the stability studies.

(b) (4)

(b) (4)

(b) (4)

Reviewer comment for section 3.2.P.5.4: The commercial lot numbers are sequential (b) (4)

All results for batch analysis under DMPQ purview (sterility), are within the pre-defined QC release acceptance criteria. Review of the other tests performed are deferred to the OVRR reviewers.

3.2.P.7 Container Closure System

The CCS and CCIT for AS01E liquid formulation, (b) (4) are described below.

CCS and CCIT for AS01E liquid formulation

Vial containers, stoppers and flip-off caps are received separately, and assembly is carried out during the filling and packaging operations.

3 mL Vials

AS01E liquid formulation is filled in 3 ml vial containers. Refer to 3.2.P.7 *Container Closure System* RSVPreF3 lyo section of this review memo for a description, tests, and acceptance criteria for the 3 mL vial containers.

13 mm Bulk Stoppers for Liquid Formulations

Stoppers are constructed of Chlorobutyl type (b) (4) rubber and are seals for container closure integrity. Stoppers can be received (b) (4) from the supplier, (b) (4) by GSK.

Alternatively, ready to sterilize (RTS) vial stoppers can be used which (b) (4) by the stopper supplier and (b) (4) by the filling site. They are product contact materials, (b) (4)

(b) (4)

The manufacturers and the representative CoA for the bulk stoppers were provided in amendment STN 125775/0.36 (eCTD 0039).

Vial Flip-off Caps

The vial flip-off caps are used to secure the stopper to the 3 mL vial filled with AS01E liquid formulation. Refer to 3.2.P.7 *Container Closure System* RSVPreF3 lyo section of

this review memo for a description, tests, and acceptance criteria for the vial flip-off caps.

Reviewer comment: *Materials of construction, critical dimensions, and generic schematic drawings for vial stoppers for liquid formulations were reviewed appear acceptable.*

CCIT

The validation of the CCIT analytical procedure was performed at (b) (4) (b) (4)) and the procedure was then (b) (4) (b) (4) The same CCIT testing was performed as for the DP. For details, refer to 3.2.P.7 *Container Closure System* for the RSVPreF3 antigen. All acceptance criteria were met.

Reviewer comment: *All results met the acceptance criteria for CCIT. The compatibility and safety evaluation data is deferred to the OVRP reviewers.*

(b) (4)

(b) (4)

(b) (4)






(b) (4)

(b) (4)

(b) (4)

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

(b) (4)



3.2.P.8 Stability

3.2.P.8.1 Stability Summary and Conclusion and 3.2.P.8.3 Stability Data

Post-approval stability protocol and stability commitment PPQ lots manufactured at (b) (4) and stability monitoring of commercial lots are reviewed here.

The following stability studies are ongoing at (b) (4) sites. During each study, 3-mL 1-dose glass Type (b) (4) vials closed by a butyl rubber stopper are stored (b) (4). The firm provided the date of Manufacture (DOM), batch sizes, data that is currently available, and study status.

- Long-term stability protocol to support the storage of AS01E FC at 5°C ± 3°C is

planned for up to (b) (4) months. Three months of data is available at this time.

Table 50: Long-Term Stability Study Acceptance Criteria (WN and ROS)

Tests	Acceptance criteria	Time point (months)
Description	Opalescent, colorless to pale brownish liquid	Release, 3, 6, 9, 12, 18, 24, 36, (b) (4)
Sterility test (b) (4)	Absence of growth	6, 12, 24, 36, (b) (4)
CCIT	(b) (4)	0 ¹ , 12, 24, 36, (b) (4)

(b) (4)

- Accelerated stability protocol to determine the rate of change of AS01E FC properties over time at (b) (4).

Table 51: Accelerated Stability Study Acceptance Criteria (b) (4)

Tests	Acceptance criteria	Time point (days)
Description	Opalescent, colorless to pale brownish liquid	(b) (4)

- (b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

For commercial lots, (b) (4) per year at each manufacturing site will be monitored for commercial stability for 36 months at $5^{\circ}\text{C} \pm 3^{\circ}\text{C}$. Tests and acceptance criteria are the same as those listed in the (b) (4) stability study table above. Description and sterility use release results as month 0 and testing is performed at months 12, 24, and 36. CCIT use results from (b) (4) testing as month 0 and testing is performed at month 36.

Reviewer comment for sections 3.2.P.8.1 and 3.2.P.8.3: Stability study status is mostly ongoing. The data that is currently available was reviewed and all tests within DMPQ purview met acceptance criteria. Review of the stability study on development lots used in clinical studies and all other stability tests and data are deferred to OVRR reviewers.

3.2.A APPENDICES

(b) (4)

(b) (4)

Table 55: Drug Product (DP) Commercial Manufacturing and Testing Facilities

Site Name	Site Address	Manufacturing / Testing Activities
GlaxoSmithKline SA (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Formulation, Filling and Lyophilization of RSVPreF3 Drug Product - Labeling, Packaging and Visual Inspection - Quality Control and Stability Testing of RSVPreF3 Final Container - Quality Control Testing of final product - Warehouse operations
(b) (4) GlaxoSmithKline Vaccines (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Labeling and Packaging - Quality Control Testing of final product - QA Release of final product - Warehouse operations
GlaxoSmithKline Vaccines (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Labeling and Packaging - Quality Control Testing of final product - Warehouse operations
GlaxoSmithKline SA (Rixensart) FEI#: 3002875226	Rue de L'Institut 89 1330 Rixensart, Belgium	<ul style="list-style-type: none"> - QA Release of final product
(b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Warehouse operations

Site Name	Site Address	Manufacturing / Testing Activities
(b) (4) FEI#: (b) (4)	(b) (4)	- Warehouse operations

Table 56: AS01E Adjuvant Commercial Manufacturing and Testing Facilities

Site Name	Site Address	Manufacturing / Testing Activities
GlaxoSmithKline SA (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Production of Intermediates - Formulation and Filling of AS01E - Labeling, Packaging and Visual Inspection - Quality Control and Stability Testing of Intermediates - Quality Control and Stability Testing of AS01E Final Container - Quality Control Testing of final product - Warehouse operations
(b) (4) GlaxoSmithKline Vaccines (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Labeling and Packaging - Quality Control Testing of final product - Warehouse operations
GlaxoSmithKline Vaccines (b) (4) FEI#: (b) (4)	(b) (4)	<ul style="list-style-type: none"> - Formulation and Filling of AS01E - Labeling, Packaging and Visual Inspection - Quality Control and Stability Testing of AS01E Final Container - Quality Control Testing of final product - Warehouse operations
(b) (4) FEI#: (b) (4)	(b) (4)	- Warehouse operations
(b) (4) FEI#: (b) (4)	(b) (4)	- Warehouse operations

GSK (b) (4), Belgium (RSVPreF3 antigen and AS01E adjuvant system)

GSK in (b) (4), Belgium is used to produce RSVPreF3 antigen and AS01E adjuvant system. The facility is composed of multiple multi-product buildings that include (b) (4)

(b) (4)

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

Reviewer comment for section 3.2.A.1: All facilities and equipment information provided appear adequate.