



DEPARTMENT OF HEALTH & HUMAN SERVICES
FDA/CBER/OVRR/DVRPA

Memorandum

Date: May 3, 2023

From: Ching Yim-Banzuelo, Program Manager
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Review Management Support Branch/DVRPA/OVRR

Through: Cassandra Overking, Branch Chief
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To: BLA STN 125775/0 File

Subject: Package & Container Labeling

Applicant: GlaxoSmithKline Biologicals

Product: Respiratory Syncytial Virus Vaccine, Adjuvanted - AREXVY

Due Date: May 3, 2023

Recommendation: Approval

Background:

This BLA for Respiratory Syncytial Virus Vaccine, Adjuvanted - AREXVY was submitted 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 submission contains the following labels that are the subject of this review:

- Single-Dose Adjuvant Suspension Component Vaccine Vial Container Label (Vial 1 of 2) (b) (4)
- Single-Dose Lyophilized Antigen Component Vial Container Label (b) (4) (Vial 2 of 2)
- Single-Dose Adjuvant Suspension Component Vaccine Vial Container Label (b) (4) (Vial 1 of 2)
- Single-Dose Lyophilized RSVPreF3 Antigen Component Vial Container Label (b) (4) (Vial 2 of 2)
- Ten Vials Adjuvant Suspension Component and Ten Vials Lyophilized RSVPreF3 Antigen Component Vial Package Label (b) (4)

These labels were reviewed for compliance with the regulations 21 CFR 201.25 & 21 CFR 207.35, Subpart G – Labeling Standards 21 CFR 610.60 (a)(1) through (7) and 21 CFR 610.60 (7) (b) through (e), 21 CFR 610.62 (a) through (c), 21 CFR 610.63, 21 CFR 610.64, 21 CFR 610.67, the Drug Supply Chain Security Act (DSCSA) and CBER Job Aid 900.08: National Drug Code, Bar Code

and Product Identifier. To ensure completeness, checklists were used during this review; however, only the checklists for the final draft labels are attached to this review (see Appendices). In each checklist, an “x” next to each item denotes that the label was found to be compliant with the corresponding regulation.

Review of package and container labels submitted September 2, 2022:

***Single-Dose Adjuvant Suspension Component Vaccine Vial Container
Label (Vial 1 of 2) (b) (4)
(NDC 58160-744-03)***

As detailed in Appendix 1, the following issues were identified:

- Verify NDC number
- Please provide the human readable data encoded by 2D barcode per Sec. 581(14)
- Please add “Respiratory Syncytial Virus, Vaccine, Adjuvanted” before AREXVY per 21 CFR 610.60 (1)
- Per 21 CFR 610.62 (b) AREXVY need to be same style and color as “...to form AREXVY”

***Single-Dose Lyophilized RSVPreF3 Antigen Component Vial Container
Label (b) (4) (Vial 2 of 2)
(NDC 58160-723-03)***

As detailed in Appendix 2, the following issues were identified:

- Verify NDC number
- Please provide the human readable data encoded by 2D barcode per Sec. 581(14).
- Please add “Respiratory Syncytial Virus, Vaccine, Adjuvanted” before AREXVY per 21 CFR 610.60 (1).
- Per 21 CFR 610.62 (b) AREXVY need to be same style and color as “...to form AREXVY”

***Single-Dose Adjuvant Suspension Component Vaccine Vial Container
Label (b) (4) (Vial 1 of 2)
(NDC 58160-744-03)***

As detailed in Appendix 3, the following issues were identified:

- Please provide the human readable data encoded by 2D barcode per Sec. 581(14)
- Please add “Respiratory Syncytial Virus, Vaccine, Adjuvanted” before AREXVY per 21 CFR 610.60 (1)

- Per 21 CFR 610.62 (b) AREXVY need to be same style and color as “...to form AREXVY”

***Single-Dose Lyophilized RSVPreF3 Antigen Component Vial Container Label (b) (4) (Vial 2 of 2)
(NDC 58160-723-03)***

As detailed in Appendix 4, the following issues were identified:

- Please provide the human readable data encoded by 2D barcode per Sec. 581(14)
- Please add “Respiratory Syncytial Virus, Vaccine, Adjuvanted” before AREXVY per 21 CFR 610.60 (1)
- Per 21 CFR 610.62 (b) AREXVY need to be same style and color as “...to form AREXVY”

***One Dose Vial Adjuvant Suspension Component and One Dose Vial Lyophilized Antigen Component Vial Package Label (b) (4)
(NDC 58160-852-12)***

The following issues were identified:

- Delete the word Recombinant throughout the labels
- Add “Combine one vial of lyophilized antigen component and one vial of adjuvant suspension component before use.”
- Replace “1 dose” to “a single dose”
- Add “After reconstitution: revise the whole paragraph
- Add “Protect AREXVY from light.”

***Ten Single-Dose Vials Adjuvant Suspension Component and Ten Single-Dose Vials Lyophilized Antigen Component Vial Package Label (b) (4)
(NDC 58160-848-11)***

As detailed in Appendix 5, no deficiencies were identified. This label is acceptable for approval.

On April 3, 2023, CBER issued several IRs to the applicant and the applicant’s responses to the carton IR on April 10, 2023; Amendment #37 were satisfactory, with the exception of CBER Comment #1 regarding the word “Recombinant” (see IR below):

(CBER) Comment 1:

Please note that we have revised the proper name of AREXVY to the following:

Respiratory Syncytial Virus Vaccine, Adjuvanted. Therefore, for all of the

Carton and Container labeling, please delete the word “Recombinant” from the proper name throughout the labels. A similar comment will be included with the package insert comments that will be emailed to you separately.

GSK’s Response to Comment 1:

GSK requests to keep “Recombinant” in the proper name as it would be beneficial for continuity and familiarity for HCPs as “Recombinant” is mentioned in other GSK and non-GSK products, i.e., Shingrix, Engerix-B, Gardasil 9. Additionally, the recently approved CPT code for the product includes the term “recombinant” (Respiratory syncytial virus vaccine, preF, recombinant, subunit, adjuvanted, for intramuscular use, (b) (4)).

(CBER) Comment 2:

For all of the Carton and Container labeling, please delete “RSVPreF3” (for simplicity) from “Lyophilized RSVPreF3 Antigen Component” throughout the labels.

GSK’s Response to Comment 2:

GSK acknowledges CBER’s request and has deleted “RSVPreF3” from “Lyophilized RSVPreF3 Antigen Component” throughout the labels.

(CBER) Comment 3:

Please verify the NDC numbers on each vial label since the numbers do not match the numbers included in the draft package insert (see Table 3 under section 16 in the package insert).

GSK’s Response to Comment 3:

- Please note that the Company does not plan to progress the 1 dose product presentation (b) (4) and is therefore proposing to delete the following draft artwork from the BLA eCTD backbone with this submission:
- Draft Carton Label 1 Antigen and 1 Adjuvant Vials (b) (4)
- Draft Container Label Adjuvant vial (b) (4)
- Draft Container Label Antigen vial (b) (4)

As the (b) (4) site has been identified as back-up site for labelling and packing activities, the draft container artwork corresponding to the 10-dose product presentation is being providing herein.

The NDC numbers provided in Section 16, Table 3 of the package insert will be updated accordingly.

(CBER) Comment 4:

For each vial label, please provide the human readable data encoded by the 2D barcode, as per Section 581 (14) in Title II of the Drug Quality and

Security Act at <https://www.fda.gov/drugs/drug-supply-chain-integrity/drug-supply-chain-security-actdscsa>.

GSK's Response to Comment 4:

The company is providing the human readable data 2D information in annex to this response.

(CBER) Comment 5:

For each antigen component vial, in the text that reads: "Reconstitute with Adjuvant Component to form AREXVY," please add the proper name "Respiratory Syncytial Virus Vaccine, Adjuvanted" in front of "AREXVY" and place AREXVY in parentheses as follows:

Reconstitute with Adjuvant Component to form Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY)

GSK's Response to Comment 5:

The proper name "Respiratory Syncytial Virus Vaccine, Adjuvanted" was added in front of "AREXVY" and AREXVY was placed in parentheses on each antigen component vial.

(CBER) Comment 6:

For each antigen component vial, please use the same font size and text color for the word "AREXVY" as used for the text before the word "AREXVY" (as indicated above). Please see the approved antigen component vial label for PRIORIX as an example.

GSK's Response to Comment 6:

Each antigen component vial was updated with the same font size and text color for the word "AREXVY" as used for the text before the word "AREXVY".

(CBER) Comment 7:

For each adjuvant component vial, in the text that will be revised to read: "Add to one vial of Lyophilized Antigen Component to form AREXVY," please use the same font size and text color for the word "AREXVY" as used for the text before the word "AREXVY." Please see the approved adjuvant component vial label for SHINGRIX as an example.

GSK's Response to Comment 7:

For each adjuvant component vial, in the text that was revised to read: "Add to 1 vial of Lyophilized Antigen Component to form AREXVY," the font size and text color for the word "AREXVY" was aligned to the text before the word "AREXVY".

(CBER) Comment 8:

Regarding both the antigen and adjuvant component vial labels, please consider making the color of the text all one color as much as possible throughout (or throughout each vial label) outside of the red box, to decrease the distraction from all the different colors. Please see the approved vial labels for PRIORIX as an example. Please comment.

GSK's Response to Comment 8:

The company has changed "Lyophilized Antigen Component" to black text on the antigen vial label, and "Adjuvant Suspension Component" to black text on the adjuvant vial label to decrease the number of colors and minimize distraction.

(CBER) Comment 1 for Carton Labels (b) (4):

Please revise the wording on the top panel from "Contents (1 dose of AREXVY):" to "Contents (a single dose of AREXVY):"

GSK's Response to Comment 1 for Carton Labels (b) (4):

As described in the response to comment 3 above, the Company does not plan to progress the 1 dose product presentation and is therefore proposing to delete the corresponding draft artwork from the BLA eCTD backbone with this submission.

(CBER) Comment 1 for Carton Labels (b) (4) :

Please revise the text in the red rectangular box on the top panel to the following: "NOTICE: Combine one vial of lyophilized antigen component and one vial of adjuvant suspension component before use."

GSK's Response to Comment 1 for Carton Labels (b) (4) :

The text in the red rectangular box on the top panel of the carton label (b) (4) for the 10-dose presentation was revised to the following: "NOTICE: Combine one vial of lyophilized antigen component and one vial of adjuvant suspension component before use."

Please note that the Company does not plan to progress the 1 dose product presentation (b) (4) and is therefore proposing to delete the corresponding draft artwork from the BLA eCTD backbone with this submission (see response to comment 3 above).

(CBER) Comment 2 for Carton Labels (b) (4) :

On the bottom panel, please revise the one paragraph to the following:

After reconstitution:

Each 0.5-mL single-dose AREXVY contains 120 mcg of recombinant respiratory syncytial virus glycoprotein F antigen (RSVPreF3) and adjuvant.

Administer AREXVY immediately or store refrigerated between 2°C and 8°C (36°F and 46°F) or at room temperature [up to 25°C (77°F)] and use within 4 hours.

Protect AREXVY from light.

GSK's Response to Comment 2 for Carton Labels (b) (4) :

The paragraph on the bottom panel of the carton label (b) (4) for the 10 dose presentation was revised as suggested by CBER.

Please note that the Company does not plan to progress the 1 dose product presentation (b) (4) and is therefore proposing to delete the corresponding draft artwork from the BLA eCTD backbone with this submission (see response to comment 3 above).

On April 17, 2023, CBER issued several IRs to the applicant and the applicant's responses to the carton IR on April 19, 2023; Amendment #40, were satisfactory with the exception of Comment #2 regarding the word "Recombinant" (see IR below):

(CBER) Comment 1:

For each antigen component vial, in the text that reads: "Reconstitute with Adjuvant Component to form AREXVY," please insert the word "Suspension" as indicated below.

Reconstitute with Adjuvant Suspension Component to form Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY)

GSK's Response to Comment 1:

GSK acknowledges CBER's request and has inserted the word "Suspension" in the text of each antigen component vial to read as follows:

Reconstitute with Adjuvant Suspension Component to form Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY)

The revised antigen vial artworks are provided in section ml.14.1 Draft Labeling.

(CBER) Comment 2:

The following two comments concerns the Package Label:

We continue to request that the proper name of AREXVY not include the word "Recombinant". Please delete the word "Recombinant" from the proper name.

GSK's Response to Comment 2:

In line with "Nonproprietary Naming of Biological Products, Guidance for Industry" (2017), the Company believes that the inclusion of "Recombinant" in the proper name of AREXVY is important in order to (1) Reflect the scientific characteristics of the vaccine and (2) avoid confusion with other technologies used for the manufacturing of vaccines (e.g., mRNA, live attenuated...). Hence, the Company proposes to keep "Recombinant" as currently proposed in US PI. This is consistent with the nonproprietary names of most vaccines published in FDA's list "Vaccines Licensed for Use in the United States", which include terms such as live, inactivated, conjugate, recombinant, mRNA, etc.

(CBER) Comment 3:

The following comment concerns the Package Label:

The Product Identifier on the carton label is split where the 2D barcode and the S/N is on one panel and the other panel has the GTIN, EXP & LOT. We recommend the S/N, GTIN, EXP and LOT information be on one panel.

GSK's Response to Comment 3:

For compliance with the Drug Supply Chain Security Act (DSCSA), a change was made to the secondary packaging for vaccine products in the vial presentation at the (b) (4) manufacturing site. The site aggregation project included an automated end-of-line operation that captures the serial number from the 2D barcode of each individual package just before inserting the package into the shipper case. This required the 2D barcode to be oriented in a certain manner so that it is visible to the case-packing equipment.

Relocation of the 2D barcode from the rear side panel of package to the top panel was deemed the only feasible technical solution to meet the below requirements. In addition, the human-readable serial number was also moved to the top panel as the overprinting technology does not allow the separation of the human-readable and 2D-barcoded serial numbers.

- Keeping the vials upright during transportation (reducing risk of glass breakage)
- Having the 2D barcodes on the packages visible when opening the shipper cases (with implementation of DSCSA, scanning operations are anticipated to be more frequent at all steps of the supply chain, and the available option of scanning a package inside the shipper case without having to remove the package would be desirable as such a manipulation could otherwise potentially modify the aggregation status of the case).

Of note, relocating the 2D barcode coupled with the human readable serial number on a panel separate from the panel containing the GTIN, EXP, and LOT information was done to comply with the DSCSA and discussed with CBER for Shingrix. CBER found this separation to be acceptable (email correspondence from Jennifer Bridgewater, CBER/OVRR/DBPAP, to Will Hoffner, GSK, on 30

September 2021). It was based on this understanding that changes were made to the secondary packaging for vaccine products in the vial presentation.

On April 21, 2023, CBER issued several IRs to the applicant and the applicant's responses to the carton IR on April 24, 2023; Amendment #43, were satisfactory.

We reference BLA 125775/0 for Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY). This information request is in reference to the AREXVY package insert and 10 doses carton container labeling that you submitted on April 19th and April 10th, respectively. Please see the attached Word document with our inserted changes and comments concerning the package insert.

The following comment concerns the Package Label:

(CBER) Comment 1:

We continue to request that the proper name of AREXVY not include the word "Recombinant". Please delete the word "Recombinant" from the proper name.

GSK's Response to Comment 1:

GSK has resubmitted the label and removed the word "Recombinant" from the proper name.

(CBER) Comment 2:

Please clarify if the 10-dose carton has any inner cartons that separate the antigen vials from the adjuvant vials.

GSK's Response to Comment 2:

In response to CBER comment #2 on the carton label, the 10-dose carton does not contain any inner cartons that separate the antigen vials from the adjuvant vials.

Recommendations

These labels are currently in compliance with 21 CFR 201.25, 21 CFR 207.35 and 21 CFR 610.60 through 21 CFR 610.67, Drug Supply Chain Security Act (DSCSA), the Guidance for Industry, "Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use," and CBER Job Aid 900.08: National Drug Code, Bar Code and Product Identifier. Therefore, these labels are recommended for approval.