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

Memorandum

Date: June 1, 2022

From: Daphne D. Stewart, CSO
RMSB, DVRPA/OVRR

Through: Tim D. Nelle, Ph.D., CAPT U.S. Public Health Service
Branch Chief, RMSB

To: BLA STN 125748/0 File

Subject: Review of GlaxoSmithKline Biologicals – BLA 125748/0
Measles, Mumps and Rubella Virus Vaccine, Live (PRIORIX)

Due Date: June 4, 2022

Actions to be taken: None. Three information requests were submitted to the firm (June 4, 2021; February 2, 2022; May 5, 2022). All deficiencies were adequately addressed.

Recommendation: Approval

Background
This BLA for Measles, Mumps and Rubella Virus Vaccine, Live (PRIORIX) was submitted for the prevention of measles, mumps, and rubella in individuals 12 months of age and older. This submission contains the following labels that are the subject of this review:

- Single-Dose 0.5 mL Vial Container Label
- Single-Dose 0.5 mL Diluent Vial Container Label
- Single-Patient-Use 0.5 mL (10 doses) Prefilled Syringe Carton Label

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 carton and container labels submitted in the original submission:

Single-Dose 0.5 mL Vial Antigen Container Label (NDC 58160-831-03):

- The applicant will need to place the NDC under the linear barcode per 21 CFR 207.33.
- The applicant will need to submit the datamatrix codes.
- The applicant will need to place the statement “Rx Only” onto the label per 21 CFR 610.60.

Single-Dose 0.5 mL Diluent Syringe Container Label (NDC 58160-833-02):

- The applicant will need to place the NDC under the linear barcode per 21 CFR 207.33.
- The applicant will need to submit the datamatrix codes.
- The applicant will need to place the statement “Rx Only” onto the label per 21 CFR 610.60.

Single-Patient-Use 0.5 mL (10 doses) Prefilled Syringe Carton Label (NDC 58160-824-15) Refer to Appendix 3:

- The applicant will need to place the NDC under the linear barcode per 21 CFR 207.33.

The above deficiencies were communicated to the applicant on June 4, 2021.

On February 2, 2022, the applicant submitted revised labels; however, these labels were not reviewed because it was expected that the applicant would be further modifying them to address concerns regarding their original proposed proprietary name (PRIORIX (b) (4)). As expected, the applicant requested that these labels be withdrawn on March 9, 2022, and submitted revised labels which included their revised proposed proprietary name (PRIORIX):

On May 5, 2022, the review committee sent the applicant the following IRs:

Single-Dose 0.5 mL Vial Antigen Container Label (NDC 58160-831-03):

a. Please replace the name “Measles, Mumps, and Rubella Vaccine, Live” (located under the NDC#) with “Lyophilized Antigen Component, Live.” Please see item b. for additional considerations.

b. Please revise:

   From: “Reconstitute with sterile water diluent provided to form (PRIORIX)”

   To: “Reconstitute with Sterile Water Diluent provided to form Measles, Mumps, and Rubella Vaccine, Live (PRIORIX)”

Since this partial container label needs to include the name expressed as either the proper or common name, the names suggested in 1.a. and 1.b. above may both be included. Alternatively, if space is limited, it may be sufficient to refer to the reconstituted vaccine as just "PRIORIX" as long as you also include the word "Live" when referring to the lyophilized antigen component. In other words, we feel that it is important to include "Live" in one name or the other if not able to include it is both places, so that users know that there is live virus in the vial.

c. Please submit the matrix code for review.

Single-Dose 0.5 mL Diluent Syringe Container Label (NDC 58160-833-02):

a. Revise to state: "Sterile Water Diluent for reconstitution to form PRIORIX"

b. Please submit the matrix code for review.

Single-Patient-Use 0.5 mL (10 doses) Prefilled Syringe Carton Label (NDC 58160-824-15):

1. Carton, Top Panel

   a. Under "Rx only," please insert a boxed notice that conveys that the vial of lyophilized antigen component must be reconstituted with the Sterile Water Diluent before use.

   b. Under "Contents: 10 Doses of PRIORIX":

      i. Revise to state: "10 single-dose vials containing Lyophilized Antigen Component, Live"

      ii. Revise to state: "10 single-dose Prefilled Ungraduated Syringes"

2. Carton, Bottom Panel

   a. Revise to state: "Reconstitution: Lyophilized Antigen Component, Live is to be reconstituted only with the accompanying Sterile Water Diluent to form Measles, Mumps, and Rubella Vaccine, Live (PRIORIX)."

   b. Revise to state: "After reconstitution, administer PRIORIX immediately. If not used immediately, store refrigerated between 2^{o} and 8^{o} C (36^{o} and 46^{o} F) and administer within 8 hours."

   c. Please add: "PRIORIX contains no preservatives."

3. Please revise side panels to be consistent with changes to the top and bottom panels.

On May 26, 2022, the applicant submitted revised labels to address the issues raised in CBER's IR dated May 5, 2022:

The revised labels for *Single-Dose 0.5 mL Vial Antigen Container Label* (NDC 58160-831-03) and *Single-Dose 0.5 mL Diluent Syringe Container Label* (NDC 58160-833-02) in the May 26, 2022, submission were reviewed (see Appendices 1, and 2 respectively). Both labels were found to be acceptable for approval. While it was noted that the NDC not directly under the linear barcode on these container labels, this was found to be acceptable based on previous consultations with OCBQ that that determined that if the NDC is in close proximity of the linear barcode that the applicant will not need to place the NDC under the linear barcode per 21 CFR 207.33.

During the review of the carton label in the May 26, 2022, submission, it was noted that the statement regarding the age indication was omitted. On May 28, 2022, CBER requested that the applicant submit a new version of this label to address this deficiency.

On June 1, 2022, the applicant submitted a revised carton label to re-add the statement "For 12 Months of Age and Older".

The revised the *Single-Patient-Use 0.5 mL (10 doses) Prefilled Syringe Carton Label* (NDC 58160-824-15) in the June 1, 2022, submission was reviewed (see Appendix 3) and was found to be acceptable.

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.

Appendix 1: Review Checklist for *Single-Dose 0.5 mL Vial Antigen Container Label* (NDC 58160-831-03) submitted May 26, 2022

21 CFR 610.60(a)(1) through (7)	**Checked items "x" indicate compliance**
a. *Full label.* The following items shall appear on the label affixed to each container of a product capable of bearing a full label:	X
* 1. The proper name of the product;	X
* 2. The name, address, and license number of manufacturer;	X
* 3. The lot number or other lot identification;	X
* 4. The expiration date;	X
* 5. The recommended individual dose, for multiple dose containers.	0.5 mL
* 6. The statement: "'Rx only'" for prescription biologicals.	X
7. If a Medication Guide is required under part 208 of this chapter, the statement required under §208.24(d) of this chapter instructing the authorized dispenser to provide a Medication Guide to each patient to whom the drug is dispensed and stating how the Medication Guide is provided, except where the container label is too small, the required statement may be placed on the package label.	N/A

21 CFR 610.62 (7) (b) through (e)	**Checked items "x" indicate compliance**
b. *Package label information.* If the container is not enclosed in a package, all the items required for a package label shall appear on the container label.	N/A
c. *Partial label.* If the container is capable of bearing only a partial label, the container shall show as a minimum the name (expressed either as the proper or common name), the lot number or other lot identification and the name of the manufacturer. In addition, for multiple dose containers, the recommended individual dose. Containers bearing partial labels shall be placed in a package which bears all the items required for a package label.	X
d. *No container label.* If the container is incapable of bearing any label, the items required for a container label may be omitted, provided the container is placed in a package which bears all the items required for a package label.	N/A
e. *Visual inspection.* When the label has been affixed to the container a sufficient area of the container shall remain uncovered for its full length or circumference to permit inspection of the contents.	X

JA 900.08: NDC, Bar Code, & Product Identifiers/21 CFR 201.25 & 21 CFR 207.35 (3)(i)	**Checked items "x" indicate compliance**
*8. Barcode Linear or One-Dimensional (1D) (Parallel Lines) NDC a. Using the website https://www.fda.gov/industry/structured-product-labeling-resources/ndcnhric-labeler-codes (to check the sponsor's NDC) b. Click "Open" c. Click "ndc_nhric_labeler_codes" d. Click "Yes" e. Locate the Firm Name and the NDC Labeler Code will be to the right	N/A N/A
*9. Product Identifier - 2D Barcode a. Locate the symbol and the datamatrix code information will consist of: NDC (01): EXPIRY (17): BATCH/LOT (10): SERIAL (21):	N/A
10. Detachable Portion If the detachable label has a 2D Barcode, then you need to follow steps #8 & steps #9 (Barcode & NDC/2D Barcode) The actual detach label needs to include: a. Proprietary Name b. NDC # c. Lot # & Expiry Date If the detachable label cannot contain all the above information, then it should have: a. Proprietary Name b. NDC # c. Lot #	N/A N/A

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 Guidance for Industry	**Checked items "x" indicate compliance**
a. Multiple-Dose b. Single-Dose c. Single-Patient-Use	x

11. *If there is an age range associated with the label, it should be included on the label. The placement should not be on the detachable portion.*	12 months of age and older.
Comments: • This label is acceptable for approval.	

**** Minimum requirement for partial labels***

Appendix 2: Review Checklist for Single-Dose 0.5 mL Diluent Syringe Container Label (NDC 58160-833-02) submitted May 26, 2022

21 CFR 610.60(a)(1) through (7)	Checked items "x" indicate compliance
b. *Full label.* The following items shall appear on the label affixed to each container of a product capable of bearing a full label:	X
* 1. The proper name of the product;	X
* 2. The name, address, and license number of manufacturer;	X
* 3. The lot number or other lot identification;	X
* 4. The expiration date;	X
* 5. The recommended individual dose, for multiple dose containers.	0.5 mL
* 6. The statement: "'Rx only'" for prescription biologicals.	X
7. If a Medication Guide is required under part 208 of this chapter, the statement required under §208.24(d) of this chapter instructing the authorized dispenser to provide a Medication Guide to each patient to whom the drug is dispensed and stating how the Medication Guide is provided, except where the container label is too small, the required statement may be placed on the package label.	N/A

21 CFR 610.62 (7) (b) through (e)	Checked items "x" indicate compliance
b. *Package label information.* If the container is not enclosed in a package, all the items required for a package label shall appear on the container label.	N/A
c. *Partial label.* If the container is capable of bearing only a partial label, the container shall show as a minimum the name (expressed either as the proper or common name), the lot number or other lot identification and the name of the manufacturer; in addition, for multiple dose containers, the recommended individual dose. Containers bearing partial labels shall be placed in a package which bears all the items required for a package label.	X
d. *No container label.* If the container is incapable of bearing any label, the items required for a container label may be omitted, provided the container is placed in a package which bears all the items required for a package label.	N/A
e. *Visual inspection.* When the label has been affixed to the container a sufficient area of the container shall remain uncovered for its full length or circumference to permit inspection of the contents.	X

JA 900.08: NDC, Bar Code, & Product Identifiers/21 CFR 201.25 & 21 CFR 207.35 (3)(i)	
*8. Barcode Linear or One-Dimensional (1D) (Parallel Lines) NDC b. Using the website https://www.fda.gov/industry/structured-product-labeling-resources/ndcnhric-labeler-codes (to check the sponsor's NDC) b. Click "Open" c. Click "ndc_nhric_labeler_codes" d. Click "Yes" e. Locate the Firm Name and the NDC Labeler Code will be to the right	N/A N/A
*9. Product Identifier - 2D Barcode a. Locate the symbol and the datamatrix code information will consist of: NDC (01): EXPIRY (17): BATCH/LOT (10): SERIAL (21):	N/A
10. Detachable Portion If the detachable label has a 2D Barcode, then you need to follow steps #8 & steps #9 (Barcode & NDC/2D Barcode) The actual detach label needs to include: a. Proprietary Name b. NDC # c. Lot # & Expiry Date If the detachable label cannot contain all the above information, then it should have: a. Proprietary Name b. NDC # c. Lot #	N/A N/A

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 Guidance for Industry	**Checked items "x" indicate compliance**
d. Multiple-Dose e. Single-Dose f. Single-Patient-Use	x

11. *If there is an age range associated with the label it should be included on the label. The placement should not be on the detachable portion.*	12 months of age and older.
Comments: • This label is acceptable for approval.	

**** Minimum requirement for partial labels***

Appendix 3: Review Checklist for Single-Patient-Use 0.5 mL (10 Dose) Prefilled Syringe Carton (Package) Label (NDC 58160-824-15) submitted on June 1, 2022

21 CFR 610.61 (a) through (s)	Checked items "x" indicate compliance
a. The proper name of the product;	X
b. The name, address, and license number of manufacturer;	X
c. The lot number or other lot identification;	X
d. The expiration date;	X
e. The preservative used and its concentration, or if no preservative is used and the absence of a preservative is a safety factor, the words "no preservative";	X
f. The number of containers, if more than one;	X
g. The amount of product in the container expressed as (1) the number of doses, (2) volume, (3) units of potency, (4) weight, (5) equivalent volume (for dried product to be reconstituted), or (6) such combination of the foregoing as needed for an accurate description of the contents, whichever is applicable;	X
h. The recommended storage temperature;	X
i. The words "Shake Well", "Do not Freeze" or the equivalent, as well as other instructions, when indicated by the character of the product;	X
j. The recommended individual dose, for multiple dose containers.	0.5 mL; 10 Dose
k. The route of administration recommended, or reference to such directions in an enclosed circular	X
l. Known sensitizing substances, or reference to an enclosed circular containing appropriate information;	X
m. The type and calculated amount of antibiotics added during manufacture;	X
n. The inactive ingredients when a safety factor, or reference to an enclosed circular containing appropriate information;	X
o. The adjuvant, if present;	N/A
p. The source of the product when a factor in safe administration;	X
q. The identity of each microorganism used in manufacture, and, where applicable, the production medium and the method of inactivation, or reference to an enclosed circular containing appropriate information	X
r. Minimum potency of product expressed in terms of official standard of potency or if potency is a factor and no U.S. standard of potency has been prescribed, the words "No U.S. standard of potency."	X
s. The statement: "'Rx only'" for prescription biologicals.	X

JA 900.08: NDC, Bar Code, & Product Identifiers/21 CFR 201.25 & 21 CFR 207.35 (3)(i)	Checked items "x" indicate compliance
9. Barcode & Linear or One-Dimensional (1D) (Parallel Lines) NDC a. Using the website https://www.fda.gov/industry/structured-product-labeling-resources/ndcnhric-labeler-codes (to check the sponsor's NDC) b. Click "Open" c. Click "ndc_hric_labeler_codes" d. Click "Yes" e. Locate the Firm Name and the NDC Labeler Code will be to the right	X X X X X X
10. Detachable Portion If the detachable label has a 2D Barcode, then you need to follow steps #8 & steps #9 (Barcode & NDC/2D Barcode) The actual detach label needs to include: a. Proprietary Name b. NDC # c. Lot # & Expiry Date	N/A
If the detachable label cannot contain all the above information, then it should have: a. Proprietary Name b. NDC # c. Lot # For 2D Barcodes on the carton label to meet the regulations for the Drug Supply Chain Security Act (DSCSA). Product Identifier - 2D Barcode a. Locate the symbol and the datamatrix codes will consist of: NDC (01): EXPIRY (17): BATCH/LOT (10): SERIAL (21):	N/A X X X X X

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 Guidance for Industry	**Checked items "x" indicate compliance**
a. Multiple-Dose b. Single-Dose c. Single-Patient-Use	x

11. *If there is an age range associated with the label it should be included on the label. The placement should not be on the detachable portion.*	For 12 months of age and older was re-added to the front panel of the carton label
Comments: This label is acceptable for approval.	