CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761255Orig2s000

PRODUCT QUALITY REVIEW(S)

LABELS AND LABELING ASSESSMENT
ADDENDUM (see pages 19 and 20)

Date of Assessment:	January 2, 2024
Assessor:	Diana Pei, PharmD Labeling Assessor Office of Biotechnology Products (OBP)
Through:	Jun Liu, PhD Product Quality Assessor OBP/Division of Biotechnology Review and Research III
Application:	BLA 761255-ORIG-2-RESUB-82
Applicant:	Fresenius Kabi USA, LLC
Submission Date:	November 4, 2022 July 7, 2023 November 27, 2023 December 28, 2023
Product:	Idacio (adalimumab-aacf)
Dosage form(s):	Injection
Strength and Container-Closure:	Proposed: 40 mg/0.8 mL single-dose glass vial kit Approved: 40 mg/0.8 mL single-dose prefilled pen (IDACIO Pen) 40 mg/0.8 mL single-dose prefilled glass syringe
Purpose of assessment:	The Applicant submitted a biologics license application for the approval of a single-dose glass vial kit to include pediatric patients who weigh 10 kg to 30 kg for juvenile idiopathic arthritis and 17 kg to less than 40 kg for Crohn's Disease.
Recommendations:	The prescribing information, medication guide, container and carton labeling are acceptable (see Appendix D) from an OBP labeling perspective.

Materials Considered for this Label and Labeling Assessment	
Materials Assessed	**Appendix Section**
Proposed Labels and Labeling	A
Evaluation Tables	B
Acceptable Labels and Labeling	C

n/a = not applicable for this assessment

DISCUSSION

We assessed the proposed labels and labeling for compliance with applicable requirements in the Code of Federal Regulations. Also, we assessed the proposed labels and labeling for consistency with recommended labeling practices (see Appendix B).

During labeling discussions, it was determined that the Instruction for Use initially proposed by the Applicant on August 7, 2023 was not needed since the vial kit is for institutional use only. The Instruction for Use is not included in the accepted labeling (see Appendix C).

CONCLUSION

The carton labeling submitted on November 27, 2023 and the prescribing information and medication guide submitted on December 28, 2023 were assessed and found to be acceptable (see Appendix C) from an OBP Labeling perspective.

APPENDICES

Appendix A: Proposed Labeling

- Prescribing Information (submitted on July 7, 2023)
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- Medication Guide (submitted on July 7, 2023)
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- Instructions for Use (submitted on August 7, 2023)
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- Carton Labeling (submitted on August 7, 2023)

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Appendix B: Evaluation Tables
Evaluation Tables: Label[1,2] and Labeling[3] Standards

Package[4] Labeling Evaluation

Proper name (package labeling)	Acceptable
Regulations: 21 CFR 610.61(a), 21 CFR 201.50(b), 21 CFR 201.10(g)(2)	✓ Yes ☐ No

[1] Per 21 CFR 1.3(b) *Label* means any display of written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.
[2] Per CFR 600.3(dd) *Label* means any written, printed, or graphic matter on the container or package or any such matter clearly visible through the immediate carton, receptacle, or wrapper.
[3] Per 21 CFR 1.3(a) *Labeling* includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.
[4] Per 21 CFR 600.3(cc) *Package* means the immediate carton, receptacle, or wrapper, including all labeling matter therein and thereon, and the contents of the one or more enclosed containers. If no package, as defined in the preceding sentence, is used, the container shall be deemed to be the package. Thus, this includes the carton, prescribing information, and patient labeling.

Recommended labeling practices (placement of dosage form outside of parenthesis and/or below the proper name)	☐ N/A

Comment/Recommendation:

Manufacturer name, address, and license number (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(b), 21 CFR 201.1(a), 21 CFR 201.1(i), 21 CFR 201.100(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (using the qualifying phrase "Manufactured by:")	

Comment/Recommendation:

Lot number or other lot identification (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(c), 21 CFR 201.18	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Expiration date (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(d), 21 CFR 201.17	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Beyond Use Date (Multiple-dose containers) (package labeling)	**Acceptable**
Recommended labeling practices: USP General Chapters: <659> Packaging and Storage Requirements and <7> Labeling	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Preservative (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(e)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Number of containers (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(f)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Product Strength (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(g), 21 CFR 201.10(d)(1), 21 CFR 201.100(b)(4)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) *USP General Chapters: <7> Labeling*	

Comment/Recommendation:

Storage temperature/requirements (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(h)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: USP General Chapters: <7> Labeling, USP General Chapters <659> Packaging and Storage Requirements	

Comment/Recommendation:

To Applicant: Remove the storage statement "(b) (4) IDACIO (b) (4) may be stored at room temperature up to a maximum of 77 F (25 C) for up to 28 days with protection from light" as no stability data was submitted to support these storage conditions for the 40 mg/0.8 mL vial.

Applicant's response:
The Applicant proposes to keep the above storage statement on the vial carton.
The stability data supporting storage of the IDACIO vial "at room temperature up to a maximum of 77 F (25 C) for up to 28 days" is now presented to the Agency (refer to Module 3, section 3.2.P.8.3.2 Stability Data – In use study – Vial).
The stability summary section has also been updated to reflect the conclusions of this study (refer to Module 3, Section 3.2P.8.1 Stability Summary and Conclusion-Vial).
Supporting Documentation
New supporting documentation
Module 3, section 3.2.P.8.3.2 Stability Data – In Use study – Vial, Replace

Module 3, section 3.2.P.8.1 Stability Summary and Conclusion-Vial, Replace Previously submitted supporting documentation *Module 3, section 3.2.P.8.3.2 Stability Data – In Use study, Vial, Sequence 0001* *Module 3, section 3.2.P.8.1 Stability Summary and Conclusions, Sequence 0069* Applicant's proposal is acceptable.

Handling: "Do Not Shake", "Do not Freeze" or equivalent (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(i)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Multiple dose containers (recommended individual dose) (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(j)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Route of administration (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(k), 21 CFR 201.5(f), 21 CFR 201.100(d)(1)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices (route of administration statement to appear after the strength statement on the principal display panel)	

Comment/Recommendation:

Known sensitizing substances (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(l), 21 CFR 801.437 (User labeling for devices that contain natural rubber)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation: The drug product is not made with latex (natural rubber latex, dry natural rubber or synthetic derivatives of natural rubber latex).

Inactive ingredients (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61, 21 CFR 201.100, FD&C Act section 502(e)	

	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091> Labeling of Inactive Ingredients, USP General Chapters <7> Labeling	

Comment/Recommendation:

Source of the product (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(p)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Minimum potency of product (package labeling)	**Acceptable**
Regulation: 21 CFR 610.61(r)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
Based on CDER's current interpretation of 21 CFR 610.61(r) and after consultation with OBP Product Quality assessors, this regulation does not apply to this product because 1) no U.S. standard of potency has been prescribed for adalimumab products (i.e., there is no specific test method described in regulation for adalimumab products that establishes an official standard of potency) and 2) Product Quality assessors have determined that potency is not a factor within the meaning of § 610.61(r) for Idacio because lot variability is not a concern as the manufacturing process is appropriately controlled to ensure the consistency and quality of the final product. Accordingly, the phrase "No U.S. standard of potency" is not required to appear on the carton labeling.

Rx only (package labeling)	**Acceptable**
Regulations: 21 CFR 610.61(s), 21 CFR 201.100(b)(1)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	

Comment/Recommendation:

Divided manufacturing (package labeling)	**Acceptable**
Regulation: 21 CFR 610.63 (Divided manufacturing responsibility to be shown)	☐ Yes ☐ No

(Also refer to the Guidance for Industry, Cooperative Manufacturing Arrangements for Licensed Biologics)	☒ N/A

Comment/Recommendation:

Distributor (package labeling)	**Acceptable**
Regulation: 21 CFR 610.64, 21 CFR 201.1(h)(5)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Bar code (package labeling)	**Acceptable**
Regulations: 21 CFR 610.67, 21 CFR 201.25	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Bar Code Label Requirements Questions and Answers* (August 2011) Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022)	

Comment/Recommendation:

Strategic National Stockpile (exceptions or alternatives to labeling requirements for human drug products) (package labeling)	**Acceptable**
Regulations: 21 CFR 610.68, 21 CFR 201.26	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

NDC numbers (package labeling)	**Acceptable**
Regulations: 21 CFR 201.2, 21 CFR 207.35	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Preparation instructions (package labeling)	**Acceptable**
Regulation: 21 CFR 201.5(g) and 21 CFR 610.61(i)	✓ Yes

Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) *USP General Chapters <7> Labeling*	☐ No ☐ N/A

Comment/Recommendation:

Package type term (package labeling)	**Acceptable**
Recommended labeling practices: 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* (October 2018) *USP chapter <659> Packaging and Storage Requirements*	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

No misleading statements (package labeling)	**Acceptable**
Regulation: 21 CFR 201.6	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Prominence of required label statements (package labeling)	**Acceptable**
Regulation: 21 CFR 201.15	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Spanish-language (Drugs) (package labeling)	**Acceptable**
Regulation: 21 CFR 201.16	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: The label does not display text in Spanish.

FD&C Yellow No. 5 and/or FD&C Yellow No. 6 (package labeling)	**Acceptable**
Regulation: 21 CFR 201.20	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: The drug product does not contain FD&C Yellow No. 5 or 6.

Phenylalanine as a component of aspartame (package labeling)	**Acceptable**
Regulation: 21 CFR 201.21(c)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: The drug product does not contain phenylalanine.

Sulfites; required warning statements (package labeling)	**Acceptable**
Regulation: 21 CFR 201.22(b)	☐ Yes ☐ No ☒ N/A

Comment/Recommendation: The drug product does not contain sulfites.

Net quantity (package labeling)	**Acceptable**
Regulation: 21 CFR 201.51	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: Guidance for Industry *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) Guidance for Industry *Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products* (June 2015) *USP General Chapters <1151> Pharmaceutical Dosage Forms (Excess volume in injections).*	

Comment/Recommendation:

Statement of Dosage (package labeling)	**Acceptable**
Regulations: 21 CFR 201.55, 21 CFR 201.100(b)(2)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Dispensing container (package labeling)	**Acceptable**
Regulation: 21 CFR 201.100(b)(7)	☐ Yes ☐ No

	☒ N/A

Comment/Recommendation:

Medication Guide (package labeling)	**Acceptable**
Regulations: 21 CFR 610.60(a)(7), 21 CFR 208.24(d)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Other (package labeling)	**Acceptable**
	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Prescribing Information Evaluation

PRESCRIBING INFORMATION

Highlights of Prescribing Information	
PRODUCT TITLE	**Acceptable**
Regulation: 21 CFR 201.57(a)(2)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: Draft Guidance for Industry on Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format (January 2018), which, when finalized, will represent FDA's current thinking on topic	

Comment/Recommendation:

Highlights of Prescribing Information	
DOSAGE AND ADMINISTRATION	**Acceptable**
Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

Highlights of Prescribing Information	
DOSAGE FORMS AND STRENGTHS	**Acceptable**
Regulations: 21 CFR 201.57(a)(8), 21 CFR 201.10, 21 CFR 201.100	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: 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* (October 2018) *USP chapter <659> Packaging and Storage Requirements* *USP General Chapters: <7> Labeling*	

Comment/Recommendation:

Full Prescribing Information	
2 DOSAGE AND ADMINISTRATION	**Acceptable**
Regulation: 21 CFR 201.57(c)(3)(iv) *Confirm appropriateness of specific direction on dilution, preparation, and administration of the dosage form and storage conditions for stability of the reconstituted or diluted drug; ensure verbatim statement for parenterals: "Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit."*	✓ Yes ☐ No ☐ N/A
Recommended labeling practices reference: USP nomenclature for diluents and intravenous solutions and storage instructions for reconstituted and diluted products; confirm the appropriateness of infusion bags, infusion sets (e.g., tubing, infusion aids, or filter membranes) incompatibilities with these components Draft Guidance *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products - Content and Format Guidance for Industry* (January 2023)	

Comment/Recommendation:

Full Prescribing Information	
3 DOSAGE FORMS AND STRENGTHS	**Acceptable**
Regulation: 21 CFR 201.57(c)(4)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: 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* (October 2018) *USP chapter <659> Packaging and Storage Requirements*	

USP General Chapters: <7> Labeling	

Comment/Recommendation:

Full Prescribing Information	
11 DESCRIPTION	**Acceptable**
Regulations: 21 CFR 201.57(c)(12), 21 CFR 610.61 (m), 21 CFR 610.61(o), 21 CFR 610.61 (p), 21 CFR 610.61 (q), FD&C Act Section 502(e)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: USP General Chapters <1091>, USP General Chapters <7>	

Comment/Recommendation:

Full Prescribing Information	
15 & 16 Hazardous Drug	**Acceptable**
Regulation: 21 CFR 201.57(c)(17)(iv) Section 15: References 1. OSHA Hazardous Drugs. OSHA. *http://www.osha.gov/SLTC/hazardousdrugs/index.html* Section 16: xxxx is a hazardous drug. Follow applicable special handling and disposal procedures.[1]	☐ Yes ☐ No ☒ N/A

Comment/Recommendation:

Full Prescribing Information	
16 HOW SUPPLIED/ STORAGE AND HANDLING	**Acceptable**
Regulation: 21 CFR 201.57(c)(17)	✓ Yes ☐ No ☐ N/A
Recommended labeling practices: to ensure placement of detailed storage conditions for reconstituted and diluted products	

Comment/Recommendation:
To Applicant: Revised sentence to clarify that storage at room temperature up to a max of 77

F for a period of 28 days with protection from light does not apply to the 40 mg/0.8 mL vial as there was no stability data to support storage of the vial in these conditions.

Applicant's response:
The Applicant proposes to keep the above storage statement on the vial carton.
The stability data supporting storage of the IDACIO vial "at room temperature up to a maximum of 77 F (25 C) for up to 28 days" is now presented to the Agency (refer to Module 3, section 3.2.P.8.3.2 Stability Data – In use study – Vial).
The stability summary section has also been updated to reflect the conclusions of this study (refer to Module 3, Section 3.2P.8.1 Stability Summary and Conclusion-Vial).
Supporting Documentation
New supporting documentation
Module 3, section 3.2.P.8.3.2 Stability Data – In Use study – Vial, Replace
Module 3, section 3.2.P.8.1 Stability Summary and Conclusion-Vial, Replace
Previously submitted supporting documentation
Module 3, section 3.2.P.8.3.2 Stability Data – In Use study, Vial, Sequence 0001
Module 3, section 3.2.P.8.1 Stability Summary and Conclusions, Sequence 0069

Applicant's proposal is acceptable.

Full Prescribing Information	
MANUFACTURER INFORMATION	**Acceptable**
Regulations: 21 CFR 201.100(e), 21 CFR 201.1	✓ Yes ☐ No ☐ N/A
Recommended labeling practices references: 21 CFR 610.61(b) (add the US license number for consistency with the carton labeling), and 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)	

Comment/Recommendation:

Medication Guide Evaluation

MEDICATION GUIDE	
TITLE (NAMES AND DOSAGE FORM)	**Acceptable**
Regulation for Medication Guide: 21 CFR 208.20(a)(7)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

MEDICATION GUIDE	
STORAGE AND HANDLING	**Acceptable**

Regulation for Medication Guide: 21 CFR 208.20(a)(2)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:
To Applicant: Revised sentence to clarify that storage at room temperature up to a max of 77 F for a period of 28 days with protection from light does not apply to the 40 mg/0.8 mL vial as there was no stability data to support storage of the vial in these conditions.

Applicant's response:
The Applicant proposes to keep the above storage statement on the vial carton.
The stability data supporting storage of the IDACIO vial "at room temperature up to a maximum of 77 F (25 C) for up to 28 days" is now presented to the Agency (refer to Module 3, section 3.2.P.8.3.2 Stability Data – In use study – Vial).
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Supporting Documentation
New supporting documentation
Module 3, section 3.2.P.8.3.2 Stability Data – In Use study – Vial, Replace
Module 3, section 3.2.P.8.1 Stability Summary and Conclusion-Vial, Replace
Previously submitted supporting documentation
Module 3, section 3.2.P.8.3.2 Stability Data – In Use study, Vial, Sequence 0001
Module 3, section 3.2.P.8.1 Stability Summary and Conclusions, Sequence 0069

Applicant's proposal is acceptable.

MEDICATION GUIDE	
INGREDIENTS	**Acceptable**
Recommended labeling practice: To ensure labeling of inactive ingredients are in alphabetical order (see USP General Chapters <1091>)	✓ Yes ☐ No ☐ N/A

Comment/Recommendation:

MEDICATION GUIDE	
MANUFACTURER INFORMATION	**Acceptable**
21 CFR 208.20(b)(8)(iii)	✓ Yes ☐ No ☐ N/A
21 CFR 610.61 (add the US license number for consistency with the carton labeling), 21 CFR 610.64 (Name and address of distributor may appear and use a qualifying phrase for consistency with the carton labeling, when applicable)	

Comment/Recommendation:

APPENDIX C. ~~Acceptable~~ Labels and Labeling (See Addendum)

- Prescribing Information and Medication Guide (submitted on December 28, 2023)
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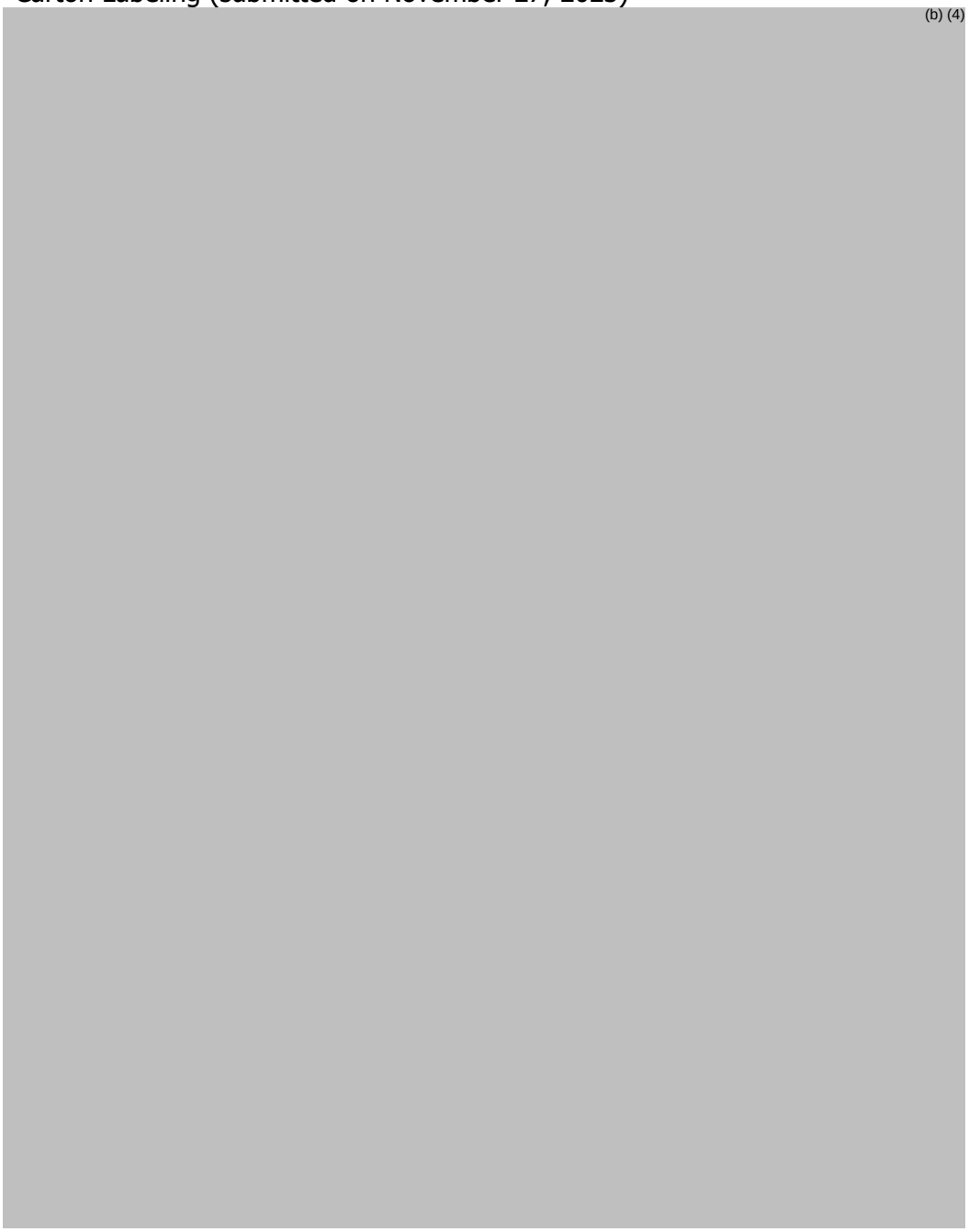
- Carton Labeling (submitted on November 27, 2023)

(b) (4)



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ADDENDUM
January 4, 2024

The Applicant submitted a proposed container label with BLA 761255-ORIG-1 (sequence 0048) for the Agency to review with this resubmission.

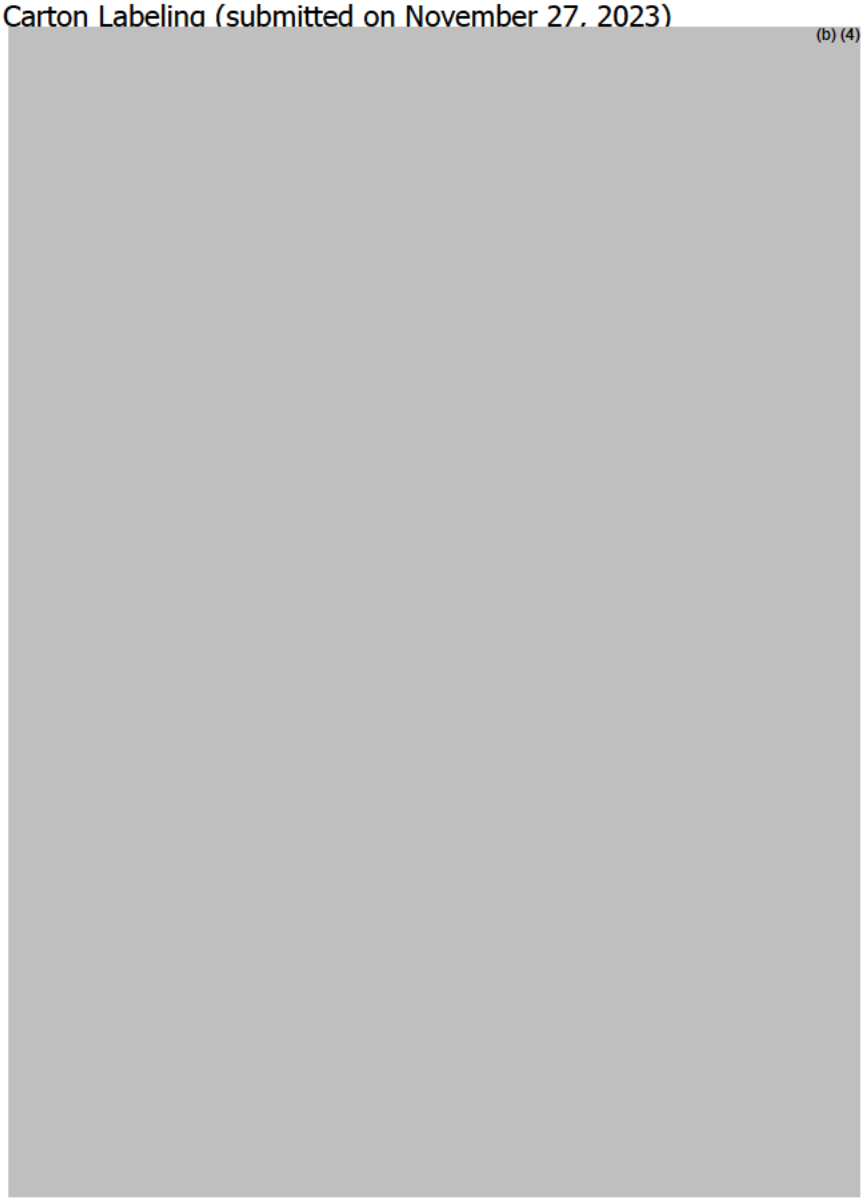
The proposed container label submitted on November 4, 2022 is acceptable from an OBP labeling perspective.

Appendix D: Accepted Labeling

- Prescribing Information and Medication Guide (submitted on December 28, 2023) \\CDSESUB1\EVSPROD\bla761255\0089\m1\us\114-labeling\114a-draft-label\draft-uspi-and-medication-guide-vial-kit-clean.docx

- Carton Labeling (submitted on November 27, 2023)

(b) (4)



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Diana Pei

Digitally signed by Diana Pei
Date: 1/04/2024 02:29:14PM
GUID: 6352da2c009ad0777a2c3b47ec094b9a

Jun Liu

Digitally signed by Jun Liu
Date: 1/04/2024 02:41:02PM
GUID: 55088b540009d43d4fb3b19bd75582e9

BLA Executive Summary
Assessment Date: 12/14/2024

1. Application/Product Information

BLA number	761255 (Original 2) for the single-dose glass vial kit
Submission Type	CR Response
Regulatory Pathway	Biosimilar 351(k)
Associated IND/BLA	IND 124098
Review Designation	Standard Review
Applicant	Fresenius Kabi USA, LLC
Indication	• Rheumatoid arthritis (RA) • Juvenile idiopathic arthritis (JIA) (2 years of age and older) • Psoriatic arthritis (PsA) • Ankylosing spondylitis (AS) • Crohn's disease (CD) in adults and pediatric patients 6 years of age and older • Ulcerative Colitis (UC) in adult patients • Plaque Psoriasis (PsO)
Rx/OTC dispensed	Rx
Drug Product Name	**Proprietary Name:** Odacio
	Non-proprietary Name/Code Name: adalimumab-aacf
	OBP Naming MAB HUMAN (IGG1) ANTI P01375 (TNFA_HUMAN) [MSB11022]
Drug Product Description	Idacio (adalimumab-aacf, MSB11022) is a recombinant human IgG1 monoclonal antibody produced in CHO cells. MSB11022 binds to Tumour Necrosis Factor-alpha (TNFα) and neutralizes its biological function by blocking its interaction with TNF Receptors, TNFR1 (p55) and TNFR2 (p75), which in turn reduces inflammatory response. Idacio is a proposed biosimilar to US-licensed Humira in the 40 mg/0.8 mL strength. Its proposed mechanism of action is the same as that of US-licensed Humira. MSB11022 drug substance (DS) is (b) (4) Idacio drug product is a sterile solution (b) (4) and supplied as a single-dose prefilled syringe (PFS) and, single-dose prefilled pen (PFP), both approved in BLA 761255 (Original 1) on December 13,

	2022 and single-dose vial kit (BLA 761255, Original 2), all at the 40 mg/0.8 mL strength.		
Dosage Form	Liquid		
Strength	• Single-dose prefilled glass syringe (PFS): 40 mg/0.8 mL • Single-dose prefilled pen (PFP): 40 mg/0.8 mL • Single-dose glass vial kit: 40 mg/0.8 mL		
Route of Administration	Subcutaneous injection		
Primary Container Closure System	**PFS**: 1 mL (b) (4) glass syringe with a 29-gauge, 12.7 mm, thin walled stainless steel needle, protected with a rigid needle shield. The syringe is closed with a (b) (4) plunger stopper (b) (4). The PFS is assembled with a (b) (4) device (a passive safety device designed to prevent needle stick injuries). **PFP**: the primary CCS for the PFP is the PFS described above. The pen assembly is a physioject disposable autoinjector (AI) device. **Vial Kit:** The vial is a (b) (4) glass vial closed with a (b) (4) rubber stopper with (b) (4) an aluminum flip off crimp seal and plastic cap. Each vial kit is supplied with a vial adapter, one sterile syringe, one sterile safety needle, two alcohol swabs.		
Co-packaged Product Information	N/A		
OPQ Review Team	**Discipline**	**Primary**	**Secondary**
	Facility	Yi Wang	Virginia Carroll
	Microbiology	Reyes Candau-Chacon	Virginia Carroll
	Drug substance and drug product	Jun Liu	Maria Gutierrez Lugo
	RBPM	Kelly Ballard	
	ATL	Maria Gutierrez Lugo	
OPQ Issued Consults	N/A		

BLA 761255/Original 1 – single-dose prefilled pen (PFP) and single-dose prefilled glass syringe (PFS) was approved as a biosimilar to US-Licensed Humira (adalimumab) on December 13, 2022. A complete response letter (CRL) was issued for BLA 761255/Original 2 – single-dose glass vial kit on the same date. Refer to BLA761255/Original 1 OPQ Executive Summary dated December 13, 2022, for the overall quality assessment of PFP, PFS and glass vial kit presentations.

The CRL identified deficiencies at the vial kit manufacturing site, [redacted] after the pre-license inspection (PLI) conducted between [redacted] This review will only focus on the adequacy of the provided response for addressing the identified deficiencies in CRL.

2. **Recommendation and Conclusion on Approvability**
   Recommendation: Approval

   The Office of Pharmaceutical Quality, CDER, recommends approval of BLA 761255/Original 2 for Idacio (MSB11022) single-dose glass vial kit, 40mg/0.8mL. The data submitted in this application are adequate to support the conclusion that the manufacture of Idacio single-dose glass vial kit is well-controlled and leads to a product that is pure and potent. It is recommended that this product be approved for human use under conditions specified in the package insert.

3. CMC Information for Action Letter
   a. Manufacturing Location:
      - Drug Substance:
        [redacted]
      - Drug Product (for single-dose glass vial kit):
        [redacted]

   b. Fill size and dosage form:
      Idacio is supplied as 40 mg/0.8 mL solution in a single-dose glass vial kit.
   c. Dating Period:
      - Drug Product: 36 months at 36°F to 46°F (2°C to 8°C). This dating period may include a single period up to 28 days at a maximum of 77°F (25°C) with protection from light.
      - Drug Substance: [redacted] months at [redacted] °C
      - Intermediate Substance, if applicable: N/A
      - For packaged products: IDACIO drug product is supplied in a carton containing 1 sterile single-use syringe, an adapter, 2 alcohol preps and 1 glass vial providing 40 mg (0.8 mL) of IDACIO
      - Stability Option: N/A
   d. Exempt from lot release:

- Yes
- Rationale, if exempted: Idacio is exempted from lot release per FR 95-29960.

4. **Basis for Recommendation**

Refer to the BLA761255/Original 1 OPQ Executive Summary dated December 13, 2022, for basis for recommendation of approval from the drug substance, drug product, immunogenicity assays, and microbiology, except for the facility for the vial presentation which are all applicable to original 2.

This memo addresses the CR issue related to deficiencies identified at the completion of the facility inspection of (b) (4)) which prevented approval of the vial presentation (original 2). Briefly, to address the deficiencies issued in the CRL, the (b) (4) facility has informed the applicant of the completion of corrective and preventive actions (CAPA) and remediation activities in response to the PLI FDA Form 483. After the (b) (4) PLI, a general GMP Inspection was conducted by the FDA at (b) (4). No observation was issued during the on-site GMP inspection. To evaluate the adequacy of the resolution of the deficiencies identified during the (b) (4) PLI, a 704(a)(4) records review request in support of BLA 761255-ORIG-2 was sent on (b) (4). Adequate descriptions of the facilities, equipment, environmental controls, cleaning and contamination control strategy were provided for (b) (4) proposed for DP vial kit manufacture. All proposed manufacturing and testing facilities are acceptable based on their current CGMP compliance status and recent relevant inspectional coverage.

5. **Life-Cycle Considerations**

Refer to the BLA761255/Original 1 OPQ Executive Summary on December 13, 2022, for life-cycle considerations.

FOIA statement: More detailed assessments of the BLA submission, which are not included in this integrated quality assessment, may be requested via a Freedom of Information Act (FOIA) request.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JUN LIU
12/15/2023 12:11:50 PM

MARIA T GUTIERREZ LUGO
12/15/2023 02:26:53 PM