CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761373Orig1s000
761425Orig1s000

OTHER REVIEW(S)

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	June 10, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe) injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., Ltd
FDA Received Date:	June 7, 2024
TTT ID #:	2023-4843-3 and 2024-8044-2
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., Ltd submitted revised container labels and carton labeling received on June 7, 2024 for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

Samsung Bioepis Co., Ltd implemented all of our recommendations and we have no additional recommendations at this time.

4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Patel, M. Label and Labeling Review for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 JUN 03. TTT ID: 2023-4843-3 and 2024-8044-2.

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MADHURI R PATEL
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YEVGENIYA M KOGAN
06/11/2024 07:34:00 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	June 3, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., LTD
FDA Received Date:	May 22, 2024
TTT ID #:	2023-4843-2 and 2024-8044-1
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined; therefore, the placeholder established name-ttwe is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., LTD submitted revised container label and carton labeling received on May 22, 2024 for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container label and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[b]

2 CONCLUSION

The container label and carton labeling are unacceptable from a medication error perspective. We note the font color used for the non-proprietary name for the 90 mg/mL has been revised to a (b) (4) color (b) (4) (b) (4) Additionally, the (b) (4) color used for the 90 mg/mL strength differentiation continues to overlap with the (b) (4) color used for the nonproprietary name for the 45 mg/0.5 mL and 130 mg/26 mL (5 mg/mL) strength carton and container.

3 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD

A. General Comments (Container Label(s) & Carton Labeling)

1. We note the font color used for the non-proprietary name for the 90 mg/mL has been revised to a (b) (4) color. (b) (4) Additionally, the 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) color which also overlap with the font color used for the non-proprietary name for the 45 mg/0.5 mL and 130 mg/26 mL (5 mg/mL) strength. Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme. We continue to recommend revising the color scheme of the 90 mg/mL strength and non-proprietary name such that all three strengths appear in their own unique colors that also do not overlap with the color used for the non-proprietary name for other strengths.

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[b] Patel, M. Label and Labeling Review Memo for Pyzchiva (BLA 761373 and BLA 761425). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 30. TTT ID: 2023-4843-1 and 2024-8044.

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YEVGENIYA M KOGAN
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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	April 30, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373 and BLA 761425
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-ttwe)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Applicant Name:	Samsung Bioepis Co., Ltd
FDA Received Date:	March 19, 2024, March 20, 2024, and April 10, 2024
TTT ID #:	2023-4843-1 and 2024-8044
DMEPA 1 Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The non-proprietary name suffix for this product has not yet been determined for BLA 761425; therefore, the placeholder ustekinumab-ttwe is used throughout this review to refer to the non-proprietary name and suffix for this product.

1 PURPOSE OF MEMORANDUM

Samsung Bioepis Co., Ltd submitted revised container labels and carton labeling received on March 19, 2024 (BLA 761373) and on March 20, 2024 (BLA 761425) and revised Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU) on April 10, 2024 (BLA 761373 and BLA 761425) and for Pyzchiva. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Pyzchiva (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[b] We previously reviewed the PI, MG, IFU, container labels and carton labeling under BLA 761373 for the 45 mg/0.5 mL and 90 mg/mL prefilled syringes and 130 mg/26 mL (5 mg/mL) vial. However, since then, Samsung Bioepis Co., Ltd submitted BLA 761425 which is intended to be specifically for the 130 mg/26 mL (5 mg/mL) vial used for the initial intravenous dose for Crohn's Disease (CD) and Ulcerative Colitis (UC), whereas the 45 mg/0.5 mL and 90 mg/mL prefilled syringe presentations will remain under BLA 761373.

2 CONCLUSION

The container labels and carton labeling are unacceptable from a medication error perspective. We note the color scheme for the revised container labels and carton labeling have been revised. However, the color scheme of the 90 mg/mL strength (b) (4) (b) (4)

3 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD

A. General Comments (Container Label(s) & Carton Labeling)

1. The 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) color (b) (4) (b) (4) Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme. We recommend revising the color scheme of the 90 mg/mL strength (b) (4) such that the strengths (b) (4) (b) (4) appear in their own unique colors (b) (4)

[b] Patel, M. Label and Labeling Review for Pyzchiva (BLA 761373). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 DEC 18. TTT ID: 2023-4843.

APPENDIX A. LABELS AND LABELING

A.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Pyzchiva labels and labeling submitted by Samsung Bioepis Co., Ltd.

- Prescribing Information, Medication Guide, and Instructions for Use received on April 10, 2024, available from \\CDSESUB1\EVSPROD\bla761373\0041\m1\us\114-labeling\114a-draft-label\sb17_bla-761373-pi-ppi-ifu-20240409_v0-11_tracked.docx and \\CDSESUB1\EVSPROD\bla761425\0005\m1\us\114-labeling\114a-draft-label\sb17_bla-761425-pi-ppi-ifu-20240409_v0-11_tracked.docx
- Container label(s) received on March 19, 2024 and March 20, 2024
- Carton labeling received on March 19, 2024 and March 20, 2024

A.2 Container Label(s) and Carton Labeling Images

Container Label(s)

4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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/s/

MADHURI R PATEL
04/30/2024 10:55:46 AM

YEVGENIYA M KOGAN
04/30/2024 02:32:09 PM

MEMORANDUM

USE-RELATED RISK ANALYSIS AND COMPARATIVE ANALYSES REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

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Date of This Review:	February 14, 2024
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373
Product Type:	Combination Product (Biologic-Device)
Product Name, Dosage Form and Strength:	SB17[1] (ustekinumab-ttwe[2]) Injection, 45 mg/0.5 mL and 90 mg/mL
Device Constituent:	Prefilled Syringe (PFS)
Rx or OTC:	Rx
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd. (Samsung)
Submission Date:	March 30, 2023, June 08, 2023
OSE TTT #:	2023-4844
DMEPA 1 Safety Evaluator:	Florence Mwangi, PharmD
DMEPA 1 Team Leader:	Murewa Oguntimein, PhD, MHS, CPH, MCHES
DMEPA 1 Deputy Director:	Jason Flint MBA, PMP

[1] SB17 has been developed as a proposed (b) (4) biosimilar to US-licensed Stelara. The proprietary name, Pyzchiva, was found conditionally acceptable by DMEPA on June 14, 2023. For the purposes of this review, "SB17" is used throughout the review to refer to this product.

[2] The nonproprietary name suffix "ttwe" was found conditionally acceptable by DMEPA on January, 26, 2024..

1 REASON FOR REVIEW

On March 30, 2023, Samsung submitted a Biologics License Application (BLA) under BLA 761373 that included a use-related risk analysis (URRA), comparative analyses (CA) and justification for not submitting Comparative Use Human Factors (CUHF) study results, to support their marketing application for SB17 (ustekinumab-ttwe) injection, 45 mg/0.5 mL and 90 mg/mL PFS, as a proposed (b) (4) biosimilar to US-licensed Stelara (hereafter, called Stelara).

2 BACKGROUND

SB17 is a single ingredient combination product with a single-dose prefilled syringe device constituent part. SB17 is human interleukin -12 and -23 antagonist intended for the treatment of:

- Patients 6 years and older with moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy.[3]
- Patients 6 years and older with active psoriatic arthritis (PsA).[3]
- Adult patients with moderately to severely active Crohn's Disease (CD).
- Adult patients with moderate to severely active Ulcerative Colitis.

On June 30, 2021, under IND 136959, Samsung submitted a URRA, CA, and justification for not submitting HF validation study results to support their future marketing application for SB17 (ustekinumab- ttwe) Injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe (PFS), as a proposed biosimilar to Stelara.

On October 5, 2021, we reviewed the aforementioned URRA, CA and justification and determined Samsung did not need to submit HF validation study results to support their future marketing application for SB17 45 mg/0.5 mL and 90 mg/mL PFS, as a proposed biosimilar to Stelara. (b) (4)

On June 30, 2023, Samsung submitted their marketing application under BLA 761373 for SB17 45 mg/0.5 mL and 90 mg/mL PFS. (b) (4) it was not clear if the product user interface of the proposed SB17 PFS evaluated in the URRA, CA and justification submitted on June 30, 2023, under BLA 761373, was identical to the product user interface of the proposed SB17 PFS evaluated in the URRA, CA and justification submitted on September 10, 2020, under IND (b) (4). Additionally, Samsung did not indicate whether the commercial product user interface had been modified

[3] SB17 PFS for use in severe plaque psoriasis and active psoriatic arthritis indications in pediatric patients (6 years or older) is proposed to be restricted to patients with a body weight of 60 kg or more who can administer whole dose of SB17 PFS.

[4] Vee, S. Use-Related Risk Analysis and Comparative Analyses review for SB17 Injection, 45 mg/0.5 mL and 90 mg/mL (IND 136959). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 05 OCT 2021. OSE RCM No.: 2021-1311.

since the June 30, 2021, submission. As such, we issued an information request (IR) on June 07, 2023, asking Samsung to specify the following:

- Specify if the product user interface of your proposed biosimilar for the US Stelara indication: Psoriasis (Ps), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis evaluated in the URRA, CA and justification submitted on June 30, 2021, is identical to the product user interface of SB17 PFS (45 mg/0.5 mL and 90 mg/mL of ustekinumab) a proposed (b) (4) biosimilar for the US Stelara indications submitted on March 30, 2023. If there are any changes, please indicate what changes you made to the user interface.

- Specify if the URRA, comparative analyses, and justification evaluated in your June 30, 2021, submission is the same as the URRA, CA, and justification submitted in your March 30, 2023, submission. If there are any changes, please specify the changes made to the URRA and CA.

Subsequently, on June 08, 2023, Samsung indicated in their IR response that they implemented changes made to their URRA, CA, and commercial product user interface since their March 30, 2023, submission. Samsung stated, "*After general advice letter dated Oct 13, 2021 (Reference ID: 4781128), there have been some changes on SB17 PFS packaging and labeling as shown below. However, these changes are minor and not expected to impact on the conclusion of comparative analyses that a HF validation study for SB17 PFS would not be needed*."

Samsung indicated the following changes were made to the SB17 URRA, CA, and labeling:

- Changed the labeling in Section 2.4 of the SB17 PFS Prescribing Information (PI) to remove the sentence (b) (4) " Samsung concluded that this sentence was removed because (b) (4).
- Changed the labeling in section 16 of the SB17 PFS PI and Instruction for use (IFU) to include information that SB17 PFS can be stored at room temperature for up to 2 months. Samsung concluded that this change was to improve the user's convenience of SB17 PFS by providing longer allowable storage period at room temperature.
- Changed the labeling in section 16 of the SB17 PFS PI to include instructions for refrigeration of the product after room temperature storage. Samsung concluded that this change was to improve the user's convenience of SB17 PFS by allowing refrigeration after room temperature storage.
- Changed the IFU to include instructions for (b) (4) the drug before use. Samsung concluded that this change was to (b) (4)
- Changed the carton opening method to pressing the open tab, breaking the perforations, and lifting up on the side flap. Samsung concluded that, "*both package designs before and after the change are commonly used and easy to open".*

- Changed the carton artwork, layout and labeling. Samsung concluded that, "*Even though the carton design has been changed, both cartons have equivalent information.*"
- Changed the container (device) label artworks and layout. Samsung concluded that, "*Changes in artwork are minor and both labels before and after change have equivalent information*."

Additionally, Samsung notes the needle gauge size as a "minor" difference. For Stelara , the PFS needle gauge size is 27-gauge regular wall fixed ½ ich needle, while the proposed SB17 PFS contains a 29 gauge thin wall fixed ½ inch needle. Samsung concluded that "*SB17 has a thinner needle (with similar inner diameter with Stelara) which could reduce potential pain from needle insertion."* We disagree with Samsung determination that the difference in PFS needle gauge size is a minor difference. We find the difference in the needle gauge size to be an "other" difference because it is likely to impact the critical tasks of performing the injection. However, in this particular instance, we find this "other" difference (thinner needle gauge size) is acceptable and this does not raise concerns that require the submission of CUHF data.

Furthermore, based on the label and labeling changes, we note these are differences between the proposed product labels and labeling, and the reference product Stelara labels and labeling. Based on our independent expert review, we determined that these labeling differences are unlikely to negatively impact user's ability to complete the critical tasks needed to use this product safely and effectively in the context of a proposed (b) (4) biosimilar product to Stelara. Therefore, we determine that these labeling differences do not warrant data from a comparative use human factors study.

3 CONCLUSION

Based on the aforementioned information, we maintain that Samsung does not need to submit human factors validation study results with their marketing application for SB17 (ustekinumab-ttwe) injection, 45 mg/0.5 mL and 90 mg/mL, PFS, a proposed biosimilar to Stelara. (b) (4) We have no HF recommendations for this marketing application.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED
APPENDIX A.
Use-Related Risk Analysis and Comparative Analyses is accessible in EDR via:

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APPENDIX B. INFORMATION REQUEST ISSUED DURING THIS REVIEW
On June 07, 2023, we issued an information request asking Samsung to clarify the following:

"We note in your March 30, 2023, submission under BLA 761373, you submitted your use-related risk analysis, comparative analyses, and justification for not submitting HF validation study results for SB17 PFS (45 mg/0.5 mL and 90 mg/mL of ustekinumab for subcutaneous injection) for the proposed indication of the US Stelara: Psoriasis (Ps), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis. And the use in Ps, PsA pediatric subjects (6 years or older) is proposed to be restricted to patients with a body weight of 60 kg or more who can administer whole dose of SB17 PFS. However, it is not clear if the product user interface of the SB17 PFS (45 mg/0.5 mL and 90 mg/mL of ustekinumab), a proposed (b) (4) biosimilar for the US Stelara indications in the URRA, CA and justification submitted on March 30, 2023 under BLA 761373, is identical to the product user interface of your proposed SB17 PFS (45 mg/0.5 mL and 90 mg/mL of ustekinumab) a proposed biosimilar for the US Stelara indication: Psoriasis (Ps), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis evaluated in the URRA, CA, and justification submitted on June 30, 2021 under IND 136959.

Please submit the following:

- Specify if the product user interface of your *proposed biosimilar* for the US Stelara indication: Psoriasis (Ps), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis evaluated in the URRA, CA and justification submitted on June 30, 2021, is identical to the product user interface of SB17 PFS (45 mg/0.5 mL and 90 mg/mL of ustekinumab) a *proposed* (b) (4) *biosimilar* for the US Stelara indications submitted on March 30, 2023. If there are any changes, please indicate what changes.

- Specify if the URRA, comparative analyses, and justification evaluated in your June 30, 2021 submission is the same as the URRA, CA, and justification submitted in your March 30, 2023, submission. If there are any changes, please specify the changes made to the Use Related Risk Analysis.

Samsung provided an acceptable response on June 08, 2023, that can be accessed in EDR via:

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/s/

FLORENCE W MWANGI
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02/14/2024 02:39:02 PM

JASON A FLINT
02/14/2024 03:04:23 PM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	December 18, 2023
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761373
Product Name, Dosage Form, and Strength:	Pyzchiva (ustekinumab-xxxx)[a] injection, 45 mg/0.5 mL and 90 mg/mL prefilled syringe and 130 mg/26 mL (5 mg/mL) vial
Product Type:	Combination Product (Biologic-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Samsung Bioepis Co., Ltd.
FDA Received Date:	March 30, 2023 and November 27, 2023
TTT ID #:	2023-4843
DMEPA 1 Acting Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Team Leader:	Yevgeniya Kogan, PharmD, BCSCP

[a] The nonproprietary name for this BLA has not yet been determined; therefore, the placeholder "ustekinumab-xxxx" is used throughout this review to refer to the non-proprietary name for this product and not intended to be included in the final labels and labeling.

1 REASON FOR REVIEW

As part of the approval process for Pyzchiva (ustekinumab-xxxx) injection, the Division of Dermatology and Dentistry (DDD) requested that we review the proposed Pyzchiva Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Labels and Labeling	F

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

The proposed Prescribing Information (PI), Medication Guide (MG), Instructions for Use (IFU), container labels and carton labeling may be improved to promote the safe use of this product from a medication error perspective. Note that DMEPA 1 is evaluating the human factors (HF) data under separate cover and based on the outcome of that review, additional label and labeling comments may be forthcoming. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for the Division and in Section 5 for Samsung Bioepis Co., Ltd..

4 RECOMMEDATIONS FOR DIVISION OF DERMATOLOGY AND DENTISTRY (DDD)

Table 2. Identified Issues and Recommendations for Division of Dermatology and Dentistry (DDD)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information (PI), Medication Guide (MG), and Instructions for Use (IFU) – General Issues			
1.	As currently presented, the proprietary name is denoted by the placeholder "SB17".	The proprietary name "Pyzchiva" was found conditionally acceptable under OSE PNR ID# 2023-1044725066 on June 14, 2023.	Replace the placeholder "SB17" in the PI, MG, and IFU with the conditionally acceptable proprietary name "Pyzchiva".
2.	The nonproprietary name suffix is denoted by the placeholder '-xxxx'.	A distinguishable nonproprietary name will facilitate accurate identification of the biological product by healthcare providers and patients.	Replace '-xxxx' with the conditionally acceptable nonproprietary name suffix when it is determined.

5 RECOMMENDATIONS FOR SAMSUNG BIOEPIS CO., LTD.

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label(s) and Carton Labeling			
1.	As currently presented, the proprietary name is denoted by the placeholder "SB17".	We are unable to assess the prominence and readability of the intended presentation of the proprietary name.	We reference our June 20, 2023 Proprietary Name Request Conditionally Acceptable letter informing you that the proprietary name, Pyzchiva, was found conditionally acceptable. We recommend replacing the placeholder "SB17" with the conditionally acceptable proprietary name, Pyzchiva, and use the intend-to-market presentation of the proprietary

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			name (font, color, etc.) so that we may adequately evaluate your labels and labeling.
2.	As currently presented, the placeholder 'xxxx' for the suffix is present as part of the nonproprietary name on the principal display panel.	A distinguishable nonproprietary name will facilitate accurate identification of the biological product by healthcare providers and patients.	Once a nonproprietary name is found conditionally acceptable for your proposed product, revise the nonproprietary name on all labels and labeling to incorporate the FDA-designated nonproprietary name suffix throughout the labels and labeling.
3.	The 90 mg/mL strength is not clearly differentiated due to the similarity between the (b) (4) colors which also overlap with the font colors used for the non-proprietary name.	Lack of adequate differentiation may contribute to wrong strength errors. Color differentiation is most effective when the color used has no association with a particular feature and there is no pattern in the application of the color scheme.	We recommend revising the color scheme of the 90 mg/mL strength or non-proprietary name such that the strengths and the non-proprietary name appear in their own unique colors that do not overlap.
4.	As currently presented, the format for the expiration date is not defined.	We are unable to assess the proposed expiration date format from a medication safety perspective.	To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*
Container Label(s)			
1.	For the 130 mg/26 mL vial, the principal display panel (PDP) is displaying duplicate strength presentations.	When the container labels are crowded, text size and prominence are generally decreased, and important information may be difficult to read or easily overlooked.	We recommend removing the product strength presentation from the top right portion of the PDP. Incorporate boxing or highlighting to increase the prominence of the product strength statement that appears under the dosage formulation, injection.
Carton Labeling			
1.	The net quantity statement does not appear on the principal display panel of the vial carton labeling.	Failure to include the net quantity statement on the principal display panel may result in confusion regarding the contents of the carton.	We recommend revising the statement “Single-dose vial” on the principal display panel include a net quantity statement [e.g., ‘One single-dose vial’ or ‘1 single-dose vial’]

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			on the principal display panel and ensure it is located away from and less prominent than the product strength. *See Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (May 2022).*
2.	The product identifier is missing.	In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format.	We recommend that you review the guidance to determine if the product identifier requirements apply to your product's labeling. See Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021). If you determine that the product identifier requirements apply to your product's labeling, we request you add a place holder to the carton labeling.
3.	For the prefilled syringe carton labeling, the terminology within the statement of dosage statement "(b) (4) is inconsistent with the	To ensure consistency with the terminology in the Prescribing Information.	We recommend revising the statement of dosage statement to read, "Recommended Dosage: see Prescribing Information."

Table 3. Identified Issues and Recommendations for Samsung Bioepis Co., Ltd. (entire table to be conveyed to Applicant) Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your human factors (HF) data.			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	terminology in the Prescribing Information.		

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for Pyzchiva that Samsung Bioepis Co., Ltd. submitted on November 27, 2023, and Stelara.

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	Stelara[b]	Pyzchiva
Initial Approval Date	September 25, 2009 (BLA 125261) September 23, 2016 (BLA 761044)	N/A
Active Ingredient	ustekinumab	ustekinumab-xxxx
Indication	Psoriasis (Ps) treatment of patients 6 years or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Psoriatic Arthritis (PsA) treatment of patients 6 years or older with active psoriatic arthritis. Crohn's Disease (CD) treatment of adult patients with moderately to severely active Crohn's disease. Ulcerative Colitis treatment of adult patients with moderately to severely active ulcerative colitis.	
Route of Administration	subcutaneous, intravenous	
Dosage Form	injection	

[b] Stelara [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2023 MAR 06. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125261s158lbl.pdf.

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	Stelara[b]	Pyzchiva
Strength	Subcutaneous: Prefilled syringe: 45 mg/0.5 mL, 90 mg/mL Vial: 45 mg/0.5 mL Intravenous: 130 mg/26 mL (5 mg/mL)	Subcutaneous: Prefilled syringe: 45 mg/0.5 mL, 90 mg/mL Intravenous: 130 mg/26 mL (5 mg/mL)

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td>Dose and Frequency</td><td>Psoriasis (Ps)
<u>Subcutaneous Adult:</u>
• For patients weighing 100 kg or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
In subjects weighing more than 100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table><tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr><tr><td>less than 60 kg*</td><td>0.75 mg/kg</td></tr><tr><td>60 kg to 100 kg</td><td>45 mg</td></tr><tr><td>more than 100 kg</td><td>90 mg</td></tr></table>*For pediatric patients weighing less than 60 kg… withdraw the appropriate volume from the single-dose vial.</td><td>Psoriasis (Ps)
<u>Subcutaneous Adult:</u>
• For patients weighing 100 kg or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
In subjects weighing more than 100 kg, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy in these subjects
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table><tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr><tr><td>60 kg to 100 kg</td><td>45 mg</td></tr><tr><td>more than 100 kg</td><td>90 mg</td></tr></table>Note: There is no dosage form for SB17 that allows weight base dosing for pediatric patients below 60 kg (132 pounds). (b) (4) [redacted]</td></tr>
</table>

<table>
<tr><th colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</th></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td></td><td>Psoriatic Arthritis (PsA)
<u>Subcutaneous Adult:</u>
• The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients with co-existent moderate-to-severe plaque psoriasis weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table>
<tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr>
<tr><td>less than 60 kg*</td><td>0.75 mg/kg</td></tr>
<tr><td>60 kg or more</td><td>45 mg</td></tr>
<tr><td>greater than 100 kg with co-existent moderate-to-severe plaque psoriasis</td><td>90 mg</td></tr>
</table>
*For pediatric patients weighing less than 60 kg… withdraw the appropriate volume from the single-dose vial.</td><td>Psoriatic Arthritis (PsA)
<u>Subcutaneous Adult:</u>
• The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
• For patients with co-existent moderate-to-severe plaque psoriasis weighing more than 100 kg, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.
<u>Subcutaneous Pediatric:</u>
Administer subcutaneously at Weeks 0 and 4, then every 12 weeks thereafter.
The recommended dose for pediatric patients (6-17 years old) based on body weight is shown below.
<table>
<tr><th>Body Weight of Patient at the Time of Dosing</th><th>Recommended Dose</th></tr>
<tr><td>60 kg or more</td><td>45 mg</td></tr>
<tr><td>greater than 100 kg with co-existent moderate-to-severe plaque psoriasis</td><td>90 mg</td></tr>
</table>
Note: There is no dosage form for SB17 that allows weight base dosing for pediatric patients below 60 kg (132 pounds). (b) (4)</td></tr>
</table>

<table>
<tr><td colspan="3">Table 4. Relevant Product Information for Listed Drug and Pyzchiva</td></tr>
<tr><td>Product Name</td><td>Stelara[b]</td><td>Pyzchiva</td></tr>
<tr><td></td><td>Crohn's Disease (CD) and Ulcerative Colitis
<u>Intravenous Induction Adult</u>:
A single intravenous infusion dose using the weight-based dosage regimen.
<table>
<tr><th>Body Weight of Patient at the time of dosing</th><th>Dose</th><th>Number of 130 mg/26 mL (5 mg/mL) vials</th></tr>
<tr><td>55 kg or less</td><td>260 mg</td><td>2</td></tr>
<tr><td>more than 55 kg to 85 kg</td><td>390 mg</td><td>3</td></tr>
<tr><td>more than 85 kg</td><td>520 mg</td><td>4</td></tr>
</table>
<u>Subcutaneous Maintenance Adult</u>:
The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td><td>Crohn's Disease (CD) and Ulcerative Colitis
<u>Intravenous Induction Adult</u>:
A single intravenous infusion dose using the weight-based dosage regimen.
<table>
<tr><th>Body Weight of Patient at the time of dosing</th><th>Dose</th><th>Number of 130 mg/26 mL (5 mg/mL) vials</th></tr>
<tr><td>55 kg or less</td><td>260 mg</td><td>2</td></tr>
<tr><td>more than 55 kg to 85 kg</td><td>390 mg</td><td>3</td></tr>
<tr><td>more than 85 kg</td><td>520 mg</td><td>4</td></tr>
</table>
<u>Subcutaneous Maintenance Adult</u>:
The recommended maintenance dosage is a subcutaneous 90 mg dose administered 8 weeks after the initial intravenous dose, then every 8 weeks thereafter.</td></tr>
</table>

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	**Stelara[b]**	Pyzchiva
How Supplied	sterile, preservative-free, colorless to light yellow solution and may contain a few small translucent or white particles. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials <u>For Subcutaneous Use</u> *Prefilled Syringes* • 45 mg/0.5 mL (NDC 57894-060-03) • 90 mg/mL (NDC 57894-061-03) Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber. *Single-dose Vial* • 45 mg/0.5 mL (NDC 57894-060-02) <u>For Intravenous Infusion</u> *Single-dose Vial* • 130 mg/26 mL (5 mg/mL) (NDC 57894-054-27)	clear, colorless to light yellow, sterile and preservative-free solution. It is supplied as individually packaged, single-dose prefilled syringes or single-dose vials <u>For Subcutaneous Use</u> *Prefilled Syringes* • 45 mg/0.5 mL (NDC XXXXX-XXX-XX) • 90 mg/mL (NDC XXXXX-XXX-XX) Each prefilled syringe is equipped with a 29 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that (b) (4) <u>For Intravenous Infusion</u> *Single-dose Vial* • 130 mg/26 mL (5 mg/mL) (NDC XXXXX-XXX-XX)

Table 4. Relevant Product Information for Listed Drug and Pyzchiva		
Product Name	**Stelara[b]**	Pyzchiva
Storage	vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. If needed, individual prefilled syringes may be stored at room temperature up to 30°C (86°F) for a maximum single period of up to 30 days in the original carton to protect from light. Record the date when the prefilled syringe is first removed from the refrigerator on the carton in the space provided. Once a syringe has been stored at room temperature, it should not be returned to the refrigerator. Discard the syringe if not used within 30 days at room temperature storage. Do not use after the expiration date on the carton or on the prefilled syringe.	vials and prefilled syringes must be refrigerated at 2°C to 8°C (36°F to 46°F). Store vials upright. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. If needed, individual prefilled syringes may be (b) (4) stored at room temperature up to 30°C (86°F) for a maximum single period of up to 60 days in the original carton to protect from light. Record the date when the prefilled syringe is (b) (4) Do not use SB17 after the expiration date on the carton or on the prefilled syringe
Container Closure	Prefilled Syringe: Each prefilled syringe is equipped with a 27 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that contains dry natural rubber Vial: N/A	Prefilled Syringe: Each prefilled syringe is equipped with a 29 gauge fixed ½ inch needle, a needle safety guard, and a needle cover that (b) (4) (b) (4) Vial: N/A

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error experiences with similar products, we reviewed the following Pyzchiva labels and labeling submitted by Samsung Bioepis Co., Ltd..

- Container Labels received on March 30, 2023
- Carton Labeling received on March 30, 2023
- Professional Sample Container Labels received on March 30, 2023
- Professional Sample Carton Labeling received on March 30, 2023
- Prescribing Information, Medication Guide, and Instructions for Use (Images not shown) received on November 27, 2023, available from \\CDSESUB1\EVSPROD\bla761373\0023\m1\us\114-labeling\114a-draft-label\uspi-v0-6-redline.pdf

F.2 Label and Labeling Images

Container label(s)

(b) (4)

[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

7 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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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/

MADHURI R PATEL
12/19/2023 10:41:17 AM

YEVGENIYA M KOGAN
12/20/2023 08:55:53 AM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: 12/14/2023

To: Strother D. Dixon, RPM, Division of Dermatology and Dentistry (DDD)

Shera C. Schreiber, Clinical Reviewer

Matthew White, Associate Director for Labeling

From: Montherson L Saint Juste, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for SB17 (ustekinumab-xxxx) injection, for subcutaneous or intravenous

BLA: 761373

Background:
In response to DDD's consult request dated May 26, 2023, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide, Instructions for Use (IFU), for the original BLA submission for SB17 (ustekinumab-xxxx) injection.

PI/Medication Guide/IFU:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on November 21, 2023, and we do not have any comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed Medication Guide and IFU, and comments were sent under separate on December 13, 2023.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling submitted by the sponsor to the electronic document room on March 30, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Montherson L. Saint Juste at Montherson.SaintJuste@fda.hhs.gov.

52 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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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/

JAMES S DVORSKY on behalf of MONTHERSON L SAINT JUSTE
12/14/2023 11:04:29 AM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	December 13, 2023
To:	Strother D. Dixon, PharmD Senior Regulatory Project Manager **Division of Dermatology and Dentistry (DDD)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Laurie Buonaccorsi, PharmD Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Montherson L. Saint Juste, PharmD, MS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG) and Instructions for Use (IFU)
Drug Name (nonproprietary name); Dosage Form and Route:	[SB17] PYZCHIVA (ustekinumab-xxxx)[1] injection, for subcutaneous or intravenous use • subcutaneous injection, 45 mg/0.5 mL or 90 mg/mL in a single-dose prefilled syringe • intravenous infusion, 130 mg/26 mL (5 mg/mL) in a single-dose vial
Application Type/Number:	BLA 761373
Applicant:	Samsung Bioepis Co., Ltd. c/o ICON Clinical Research, LLC

[1] SB17 was developed as a proposed biosimilar to US-licensed Stelara (ustekinumab) BLA 125261 and BLA 761044. The proposed Tradename PYZCHIVA was found to be conditionally acceptable by the Division of Medication Error Prevention and Analysis I (DMEPA 1) on June 20, 2023. The nonproprietary name suffix has not been determined at this time and we therefore use the placeholder "-xxxx" for the 4-letter nonproprietary name suffix.

1 INTRODUCTION

On March 30, 2023, Samsung Bioepis Co., Ltd. c/o ICON Clinical Research, LLC submitted for the Agency's review an original Biologics License Application (BLA) 761373 for [SB17] PYZCHIVA (ustekinumab-xxxx) injection, a proposed (b) (4) biosimilar to US-licensed STELARA (ustekinumab) injection [BLA 125261 and BLA 761044] for the treatment of the following:

- patients 6 years or older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy
- patients 6 years or older with active psoriatic arthritis
- adults with moderately to severely active Crohn's Disease
- adults with moderately to severely active ulcerative Colitis

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Dermatology and Dentistry (DDD) on May 26, 2023, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) and Instructions for Use (IFU) for [SB17] PYZCHIVA (ustekinumab-xxxx) injection.

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and a separate DMEPA review of the IFU will be forthcoming.

2 MATERIAL REVIEWED

- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection MG received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection single-dose prefilled syringe IFU, received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Draft [SB17] PYZCHIVA (ustekinumab-xxxx) injection Prescribing Information (PI) received on March 30, 2023, revised by the Review Division throughout the review cycle, and received by DMPP on November 22, 2023.
- Approved US-licensed STELARA (ustekinumab) injection MG dated March 6, 2023, and IFU dated April 6, 2020.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the IFU, the target reading level is at or below an 8th grade level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using

fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the MG and IFU documents using the Arial font, size 10.

In our collaborative review of the MG and IFU we:

- simplified wording and clarified concepts where possible
- ensured that the MG and IFU are consistent with the PI
- removed unnecessary or redundant information
- ensured that the MG and IFU are free of promotional language or suggested revisions to ensure that they are free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- evaluated the MG and IFU per the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the MG and IFU are consistent with the approved labeling for US-licensed STELARA (ustekinumab) injection where applicable.

4 CONCLUSIONS

The MG and IFU are acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the MG and IFU is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the MG and IFU.

Please let us know if you have any questions.

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/

LAURIE J BUONACCORSI
12/13/2023 03:05:57 PM

MONTHERSON L SAINT JUSTE
12/13/2023 03:24:39 PM

LASHAWN M GRIFFITHS
12/13/2023 04:51:20 PM

OFFICE OF PRODUCT EVALUATION AND QUALITY
OFFICE OF HEALTH TECHNOLOGY 3

DIVISION OF DRUG DELIVERY, GENERAL HOSPITAL & HUMAN FACTORS

INTERCENTER CONSULT MEMORANDUM – STREAMLINED

Date:	12/11/2023		
To:	Kristine Leahy		
Requesting Center/Office:	CDER/OPQ	Clinical Review Division: OPRO/DRBPMI/RBPMB1	Other
From:	Sangeetha Rajesh OPEQ/OHT3/DHT3C		
Through (Division): *optional	Shruti Mistry, Assistant Director OPEQ/OHT3/DHT3C		
Subject:	Consult for Submission: Technical engineering/Device design A CDRH consult is requested for the final drug product which is a pre-filled syringe (PFS) with a safety feature.		
Recommendation:	**Note to CDER:** The device constituent appears to be a non-emergency PFS and it is assembled into a needle safety device. (b) (4) (b) (4) (b) (4) The evaluation of PFS performance is deferred to CDER per the ICCR Agreement. The device's safety performance has been assessed and deemed satisfactory. The device has also met all the Essential Performance Requirements. The 6-month accelerated aging study supports the sponsor's claim of 24-month shelf life, which is acceptable.		

Digital Signature Concurrence Table		
Reviewer	**Team Lead (TL)**	**Division (optional)**
Sangeetha Rajesh -S 2023.12.11 13:50:32 -05'00'	Shruti N. Mistry -S	Digitally signed by Shruti N. Mistry -S Date: 2023.12.11 16:20:54 -05'00'

1. SUBMISSION OVERVIEW

Table 1. Submission Information	
Consult Identification #	ICCR# 00918234
Consult Request Link	https://force-dsc.lightning.force.com/lightning/r/Case/5003d0000087puQAAQ/view

ICC tracking #	ICC2300410
Submission Number	BLA 761373
Sponsor	Samsung Bioepis Co., Ltd.
Drug/Biologic	SB17, a proposed (b) (4) biosimilar to Stelara
Indications for Use	Psoriasis (Ps), Psoriatic Arthritis (PsA), Crohn's Disease (CD), and Ulcerative Colitis.
Device Constituent	Pre-filled syringe with safety feature
Related Files	

2. CDRH REVIEW

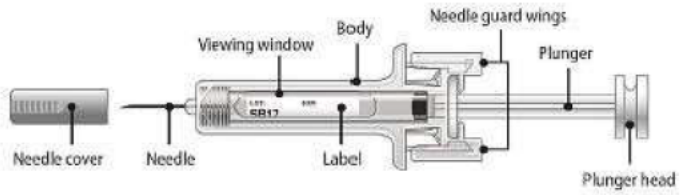
ICC Review Request from CDER/OPQ, Other:	Janell Artis, CDER/OPQ/OPRO/DRBPMI/RBPMB1
Device Presentation(s) being evaluated:	Pre-filled syringe with safety feature
Objective of this Memo:	Consult for Technical engineering/Device design
Review **Comments**:	For the PFS-S, the review was focused on the performance characteristics of PFS and the needle safety feature.
Review **Recommendation**:	The device's safety performance has been assessed and deemed satisfactory. The device has also met all the Essential Performance Requirements. The 6-month accelerated aging study supports the sponsor's claim of 24-month shelf life, which is acceptable.

Device description:

The SB17 is presented as a pre-filled syringe (PFS). The PFS is a single use, disposable injection device containing SB17 active substance (ustekinumab) for subcutaneous injection. SB17 PFS is provided in two strengths: 45 mg of ustekinumab in 0.5 mL solution and 90 mg of ustekinumab in 1.0 mL solution and as a single-use vial containing 130 mg ustekinumab in 26 mL solution for intravenous infusion.

SB17 pre-filled syringe (PFS) DP is a clear, colorless to light yellow, sterile and preservative-free solution for injection. SB17 PFS DP is provided in the following two strengths: 45 mg/0.5 mL and 90 mg/1.0 mL. Both SB17 45 mg and 90 mg solution for injection are presented as a single-use safety PFS for subcutaneous injection.

SB17 Safety PFS is intended for use in subcutaneous administration of drug by healthcare providers, and caregivers and patients who received proper training on subcutaneous injection. The SB17 Safety PFS is provided fully assembled with the PFS containing a 45 mg or 90 mg of SB17 ustekinumab for injection. The requirements set forth in 21 CFR 820.30 concerning design controls for medical devices have been implemented to the design and development process of SB17 Safety PFS.



The primary packaging components of SB17 Safety PFS consist of a 1 mL clear glass syringe with staked needle, rigid needle shield, and plunger stopper. The glass syringe, as the primary container closure, contains SB17 DP. The Safety PFS consists of a nude PFS assembled into secondary packaging components including safety shield and plunger rod.

SB17 Safety PFS is a biologic-device combination product within the meaning of Quality System Regulation [21 CRF part 3.2 (e)], where the drug product (DP) provides the primary mode of action.

Primary packaging:

The primary packaging material for PFS consists of a glass syringe and a rubber stopper. The description and quality standards are summarized in Table 2.

Table 2: Materials of Construction of SB17 Safety PFS Primary Packaging

Component		Material	Description	DMF No.
Syringe	Syringe barrel	Glass	Ph. Eur. 3.2.1, USP <660>	(b) (4)
	Hypodermic needle	Stainless steel	ISO 9626	
				(b) (4)
	Rigid needle shield	(b) (4) (rigid shield) Elastomer (needle shield)	Elastomer: Ph. Eur. 3.2.9, USP <381>	
Stopper	Plunger stopper	Rubber	Ph. Eur. 3.2.9, USP <381>	
				(b) (4)

Representative drawings of the syringe and stopper with the dimensions is provided in Figure 4 and 5.

Figure 4: Representative Drawing of the Syringe

Secondary Packaging:

The secondary packaging consists of a safety shield and a plunger rod. The safety shield is (b) (4) which has 510k cleared (b) (4) as an anti-needlestick safety device. The description of the secondary packaging materials is summarized in Table 3.

Table 3: Materials of Construction of SB17 Safety PFS Functional Secondary Packaging

Component	Material	Description
Safety shield	(b) (4)	Passive needle guard systems to reduce the occurrence of accidental needlestick injury

Component	Material	Description
Plunger rod	(b) (4)	Molded plastic component for a manual use in direct injection

The schematic diagram of the safety shield and plunger rod are provided in Figure 6 and 7.

Figure 6: Representative Schematic Diagram of the Safety Shield

Figure 7: Representative Schematic Diagram of the Plunger Rod

Non functional secondary packaging consists of a carton box, tray and a leaflet.

Performance Testing:

The sponsor has evaluated all the Essential Performance Requirements for a PFS-S syringe but did not provide justification for the sample size selected to show that the device performs at an acceptable reliability. An IR was sent to the sponsor to provide additional analysis of your data to demonstrate that the results obtained from the number of samples tested support an acceptable reliability.

The sponsor provided the following information regarding sample size, confidence and reliability and the EPR's tested.

SB17 Safety PFS was subjected to design verification test (DVT), in accordance with ISO 11608-1:2022 and all results well met the acceptance criteria.

(b) (4)

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(b) (4)

Reviewer Comment:
The design verification and validation studies for the PFS-S performed by the sponsor are acceptable and no additional data is required. The sponsor provided performance testing data for all the EPRs with an adequate sample size and demonstrated that the results obtained from the number of samples tested support an acceptable reliability, additional statistical analysis of the data, including *k* value, confidence and reliability.

Sharps Injury Prevention:

In order to confirm the sharps prevention feature of SB17 safety shield, sharps injury prevention study (needle safety device performance verification) was conducted by safety shield supplier. Total of 500 safety shields filled with saline solution were tested, all injections were completed successfully, and the safety device activated and locked in all devices preventing any accidental needle stick injury.

50 participants were selected to test 10 devices each, for a total of 500 Safety PFS filled with saline solution. The 50 user participants consisted of 20 health care professionals (HCPs), notably nurses, and 30 self-injecting patients (SIPs). Participants were chosen as representative of the population of intended users; demographics met the inclusion criteria as per the protocol (Table 32).

Table 32: Chosen participants as representative of the population of intended users.

User Group	Inclusion Criteria (underline) and Demographics	Number of Participants
HCP	- HCP from different facilities: 100% hospital, 5% private practice, 5% medical clinic, 5% other. - HCP from different practice types: 55% registered nurses, 5% clinical specialist, 5% oncology specialist, 5% hepatology specialist, 15% other. - Performing a minimum of 20 injections per month: 80% gave more than 20 injections per month.	20
	- Experience in medication injection for rheumatoid arthritis, multiple sclerosis, Crohn's disease, cancer and psoriasis. - Right/left handedness representative of human population: 90% were right handed. - 90% of nurses had small or extra-small hands. - 45% had prior experience of needlestick injury.	

SIP	- Adult and elderly patients: 77% were aged between 18 and 55 years old, 23% were aged +55years old. - To include both male & female: 67% were female. - Diagnosis of multiple sclerosis (47%), rheumatoid arthritis (23%), Crohn's disease (13%), cancer (7%), asthma (3%), 7% other (psoriasis, or multiple diagnosis of the above). - Performing a minimum of 2 injections per month: ranged from 1-2 to 16 injections per month - Mix of new (< 6 mo) and experienced (> 6 mo) self-injecting users: 77% were experienced. - Right/left handedness representative of human population: 95% were right handed.	30

Total of 500 safety shield filled with saline solution were tested, in all injections were completed successfully and the safety device activated in all, therefore zero failures were recorded.

Reviewer Comment:
The simulated clinical study performed to assess the safety feature of the PFS-S is acceptable. According to Table F.1 in Annex F of ISO 11608-1:2022, recommended sample size for attribute tests is 300 for 95% confidence with 99% probability and the sponsor has tested with 500 Safety PFS and shown to have zero failures.

Stability of PFS

Stability Summary and Conclusion:

SB17 45 mg and 90 mg Safety PFS batches were placed on accelerated aging stability at the accelerated storage condition of 23-27°C/55-65% RH and real-time aging stability at the long-term storage condition of 2-8°C. The accelerated aging study condition is intended to provide sufficient evidence for shelf life claim of the Safety PFS until data from real-time aging studies are available in accordance with ASTM F1980.

The stability program for SB17 Safety PFS is summarized in Table 10. The details on each study type are provided in this section.

Table 10: Stability Program of SB17 Safety PFS

Study Type	Presentation	Batch No.	Storage Conditions	Data Available (Month)[a]
Accelerated aging study 1[b]	45 mg PFS	363444_00001 363444_00002 363444_00003	23-27°C, 55-65% RH	**0, 1 (RTE 4 mo)**, 3 (RTE 1 yr)
	90 mg PFS	363445_00001 363445_00002 363445_00003		
Accelerated aging study 2[c]	45 mg PFS	363444_00001_PQ 363444_00002_PQ 363444_00003_PQ	23-27°C, 55-65% RH	**0[d]**, 3 (RTE 1 yr), 6 (RTE 2 yr), 12 (RTE 4 yr)

	90 mg PFS	363445_00001_PQ 363445_00002_PQ 363445_00003_PQ		
Real time aging study[c]	45 mg PFS	363444_00001_PQ 363444_00002_PQ 363444_00003_PQ	2-8°C	**0**, **1**, 3, 6, 12, 24, 36, 48[e]
	90 mg PFS	363445_00001_PQ 363445_00002_PQ 363445_00003_PQ		

RTE: real time equivalent
[a] Completed time points are in bold.

(b) (4)

d Initial time point results for real time aging study were used for the initial time point for accelerated aging study 2.
[e] At 24, 36, and 48 month time points, the Safety PFS is stored at room temperature (RT) for additional 1 month to support the in-use storage condition and duration for patient convenience.

Stability Protocol:

The stability protocol proposed by the sponsor is represented in Tables 11, 12 and 13.

Table 11: Stability Testing Schedule for Accelerated Aging Study 1

Test	**Acceptance Criteria**	**Test Interval (Month)**		
		0	**1 (RTE 4 months)**	**3 (RTE 1 year)**
Visual inspection	Pass	X	X	X
Cap removal force	(b) (4)	X	X	X
Break-loose force		X	X	X
Gliding force		X	X	X
Safety-shield activation force		X	X	X
Delivered volume		X	X	X
Confirm the lock after safety-shield activation	Pass	X	X	X

Container closure integrity test (CCIT)	Pass	N/A	X	X

Table 12: Stability Testing Schedule for Accelerated Aging Study 2

Test	Acceptance Criteria	Test Interval (Month)			
		0[a]	3 (RTE 1 year)	6 (RTE 2 years)	12 (RTE 4 years)
Visual inspection	Pass	X	X	X	X
Cap removal force	(b) (4)	X	X	X	X
Break-loose force		X	X	X	X
Gliding force		X	X	X	X
Safety-shield activation force		X	X	X	X
Delivered volume		X	X	X	X
Confirm the lock after safety-shield activation	Pass	X	X	X	X
Container closure integrity test (CCIT)	Pass	X	N/A	X	X

[a] Initial time point results for real time aging study were used for the initial time point.

Table 13: Stability Testing Schedule for Real-time Aging Study

Test	Acceptance Criteria	Test Interval (Month)							
		0	1	3	6	12	24[a]	36[a]	48[a]
Visual inspection	Pass	X	X	X	X	X	X	X	X
Cap removal force	(b) (4)	X	X	X	X	X	X	X	X
Break-loose force		X	X	X	X	X	X	X	X
Gliding force		X	X	X	X	X	X	X	X
Safety-shield activation force		X	X	X	X	X	X	X	X
Delivered volume		X	X	X	X	X	X	X	X
Confirm the lock after safety-shield activation	Pass	X	X	X	X	X	X	X	X
Container closure integrity test (CCIT)	Pass	X	N/A	N/A	N/A	X	X	X	X

[a] At 24, 36, and 48 month time points, the PFS is stored at room temperature (RT) for additional 1 month to support the in-use storage condition and duration for patient convenience.

The proposed shelf-life for SB17 Safety PFS is 24 months when stored at 2-8°C. This shelf-life is based on the 6 months stability data of accelerated aging study 2 that will become available during the review process. In accordance with ASTM F1980, the data obtained from accelerated condition can be extrapolated to 4-fold. The stability data have conformed to the acceptance criteria at the accelerated aging condition for up to 1 month, which is equivalent to 4 months of real-time aging.

The CDER CMS reviewer proposed looking at Supplements 15 and 17 for additional stability data provided by the sponsor. However, the supplemental data does not have any information regarding the EPR's tested at the various end points. So, the data provided so far only supports a shelf life claim of (b) (4) months.

An IR was sent to the sponsor on Dec 6,2023 to provide the additional stability data to claim the 24-month shelf life or direct us to the submission that carries this information.

The sponsor has provided the response to the IR on Dec8,2023.

The functional stability data of SB17 Safety PFS are reported in Section 3.3.2. Functional performance is maintained up to 6 months from the Safety PFS assembly at accelerated condition, which is equivalent to 24 months at long term storage condition. The functional stability study will be continued up to the end of proposed shelf life.

(b) (4)

[redacted]

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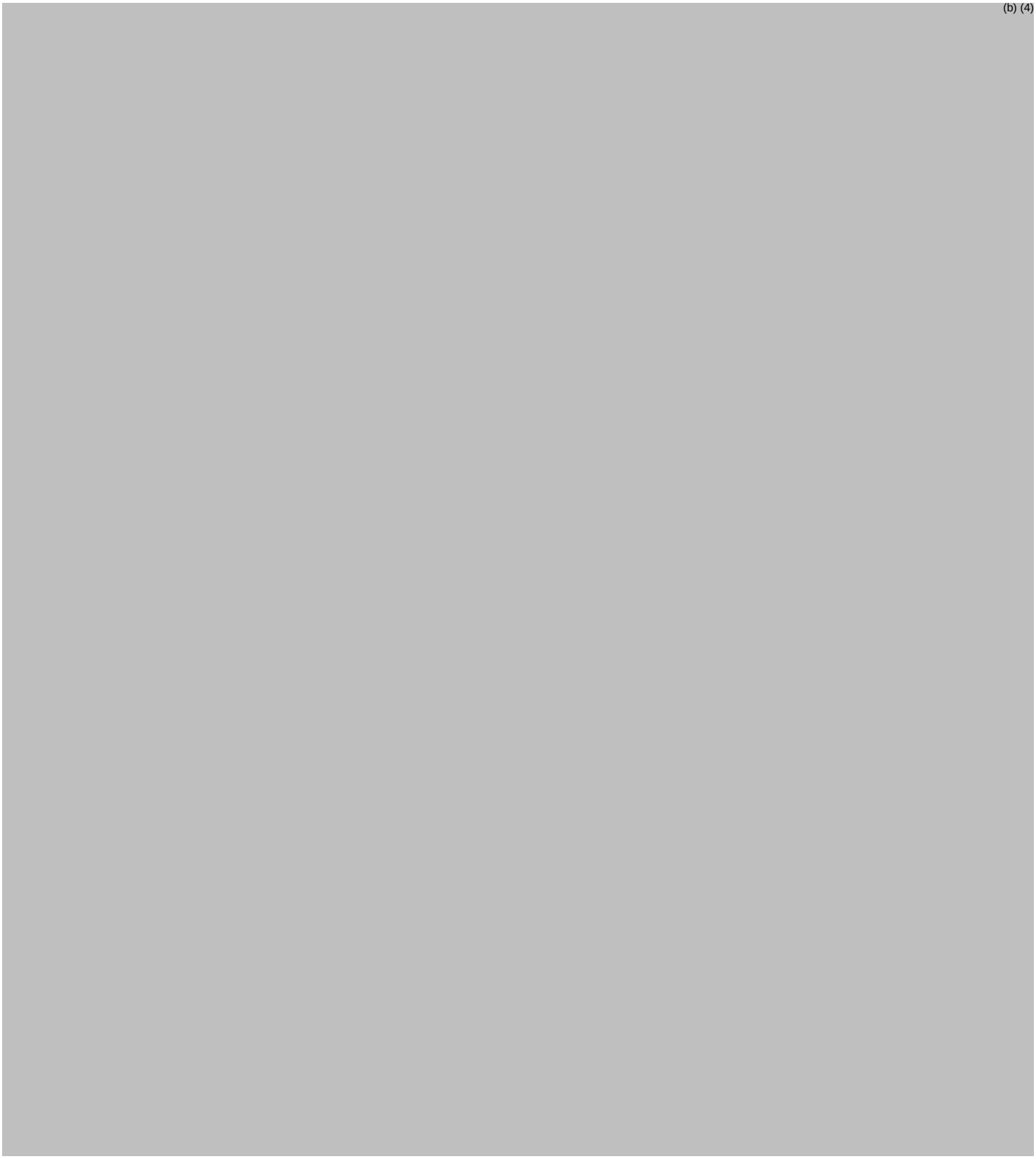
(b) (4)



Reviewer Comment:

Samsung Bioepis has provided the updated functional stability study data on essential performance requirements (EPR's) tested up to 6 months under the accelerated aging and real time aging conditions.

The stability data obtained from 6 months under accelerated aging condition are equivalent to 24 months under real time aging condition, and the data supports the proposed shelf-life of 24 months for SB17 Safety pre-filled syringe (PFS) drug product (DP) and the results are acceptable.

Shelf life and Storage Conditions:

The proposed shelf life for PFS DP is 24 months when stored at 5 ± 3°C. This shelf life is based on the stability data of three clinical phase DP batches that will become available during the review process.

The sponsor claims that the clinical phase DP batches are considered representative of the commercial batches and therefore can be used for shelf-life claim. Although there were limited number of process changes between the clinical phase and PPQ/commercial DP manufacturing process, all those changes were assessed to have low risk.

The comparability between clinical phase and PPQ batches has been demonstrated by the sponsor in the submission in section 3.2.P.5.6 Justification of Specifications. The material and biocompatibility evaluation for both clinical and commercial PFS has also shown to be comparable as demonstrated in Section 3.2.R.6 Medical Devices.

Reviewer Comment:

Based on the comparability data provided by the sponsor, clinical phase DP batches can be considered appropriate for establishing the shelf life claim as requested by the sponsor.

---END OF REVIEW---

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 6/16/2023

TO: Division of Dermatology and Dentistry (DDD)
Office of Immunology and Inflammation (OII)

FROM: Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct an on-site inspection**

RE: BLA 761373

The Office of Study Integrity and Surveillance (OSIS) determined that an inspection is not needed for the site listed below. The rationale for this decision is noted below.

Rationale

(b) (4): OSIS conducted a Remote Regulatory Assessment (RRA) for the analytical site in (b) (4). The RRA was conducted under the following submission: NDA (b) (4).

The following objectionable condition was observed:

(b) (4)

Site

Facility Type	Facility Name	Facility Address
Analytical	(b) (4)	

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/

JOSHUA L PEREZ
06/22/2023 04:47:20 PM