CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761173Orig1s000

OTHER REVIEW(S)

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:	July 14, 2022
To:	Courtney Hamilton, PharmD, BCPS Regulatory Project Manager **Division of Non-Malignant Hematology (DNH)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Susan Redwood, MPH, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Jina Kwak, PharmD, RAC Team Leader **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI) and Instructions for Use (IFU)
Drug Name (nonproprietary name):	STIMUFEND (pegfilgrastim-fpgk)[1]
Dosage Form and Route:	injection, for subcutaneous use
Application Type/Number:	BLA 761173
Applicant:	Fresenius Kabi USA, LLC

[1] STIMUFEND has been developed as a proposed biosimilar to US-licensed NEULASTA (pegfilgrastim). The proposed proprietary name STIMUFEND was conditionally acceptable on June 19, 2020. The proposed nonproprietary name "pegfilgrastim-fpgk" was conditionally acceptable by DMEPA on February 1, 2021 and is used throughout this document.

1 INTRODUCTION

On March 27, 2020, Fresenius Kabi USA, LLC submitted for the Agency's review an original Biologics License Application (BLA) 761173 for STIMUFEND (pegfilgrastim-fpgk) injection. The proposed indication for STIMUFEND (pegfilgrastim-fpgk) is to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. This application is a proposed biosimilar to NEULASTA (pegfilgrastim), injection, for subcutaneous use (BLA 125031).

On May 18, 2022, Fresenius Kabi USA, LLC submitted a revised STIMUFEND (pegfilgrastim-fpgk) injection, Instructions for Use (IFU) in response to an Agency's request dated April 21, 2022, for the Applicant to edit their proposed IFU text to align with the US-licensed NEULASTA prefilled syringe IFU. This request was made in accordance with the Agency's recommendations in the Labeling for Biosimilar Products Guidance.

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 Non-Malignant Hematology (DNH) on June 22, 2022, and June 21, 2022, respectively, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for STIMUFEND (pegfilgrastim-fpgk) injection, for subcutaneous use.

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 STIMUFEND (pegfilgrastim-fpgk) injection PPI received on March 27, 2020 and March 5, 2021, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 13, 2020 and June 23, 2022.
- Draft STIMUFEND (pegfilgrastim-fpgk) injection IFU received on May 18, 2022, and received by DMPP and OPDP on June 23, 2022.
- Draft STIMUFEND (pegfilgrastim-fpgk) Prescribing Information (PI) received on March 5, 2021, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 23, 2022.
- DMPP and OPDP STIMUFEND (pegfilgrastim-fpgk) review of draft PPI and IFU dated November 19, 2020.
- Approved US-licensed NEULASTA (pegfilgrastim) injection, (BLA 125031) labeling dated February 2, 2021.

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.

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.

In our collaborative review of the PPI and IFU we:

- simplified wording and clarified concepts where possible
- ensured that the PPI and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI and IFU are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI and IFU meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI and IFU are consistent with the approved comparator labeling where applicable.

4 CONCLUSIONS

The PPI 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 PPI and IFU are 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 PPI and IFU.

Please let us know if you have any questions.

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/s/

SUSAN W REDWOOD
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JINA KWAK
07/14/2022 12:31:58 PM

BARBARA A FULLER
07/14/2022 12:49:48 PM

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

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

Memorandum

Date: July 7, 2022

To: Courtney Hamilton, PharmD, BCPS, Regulatory Project Manager, Division of Nonmalignant Hematology (DNH)

Virginia Kwitkowski, MS, ACNP-BC, Associate Director for Labeling, (DNH)

From: Melissa Khashei, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Jina Kwak, PharmD, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for STIMUFEND® (pegfilgrastim-fpgk) injection, for subcutaneous use

BLA: 761173

In response to DNH's consult request dated June 21, 2022, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), instructions for use (IFU) and carton and container labeling for the original BLA submission for STIMUFEND® (pegfilgrastim-fpgk) injection, for subcutaneous use

PI: OPDP's comments on the proposed labeling are based on the draft labeling received by electronic mail from DNH (Courtney Hamilton) on July 5, 2022, and are provided below.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by electronic mail from DNH (Courtney Hamilton) on July 5, 2022, and we do not have any comments.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI and IFU will be sent under separate cover.

Thank you for your consult. If you have any questions, please contact Melissa Khashei at (301) 796-7818 or Melissa.Khashei@fda.hhs.gov.

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/s/

MELISSA KHASHEI
07/07/2022 09:31:13 AM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	March 1, 2021
Requesting Office or Division:	Division of Nonmalignant Hematology (DNH)
Application Type and Number:	BLA 761173
Product Name and Strength:	Stimufend (pegfilgrastim-fpgk) injection 6 mg/0.6 mL
Applicant/Sponsor Name:	Fresenius Kabi
FDA Received Date:	February 19, 2021
OSE RCM #:	2020-621-1
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

1 PURPOSE OF MEMORANDUM

Fresenius Kabi submitted revised container label and carton labeling for Stimufend (pegfilgrastim-fpgk) on February 19, 2021 (Appendix A). The revisions are in response to recommendations that we made during a previous label and labeling review.[a] We reviewed the revised label and labeling to determine if they are acceptable from a medication error perspective.

2 DISCUSSION AND CONCLUSION

We note that our previous recommendations were implemented. We conclude the revised container label and carton labeling are acceptable from a medication error perspective. We have no additional recommendations at this time.

[a] DeGraw, S. Label and Labeling Review for Stimufend [MSB11455] (pegfilgrastim-xxxx) BLA 761173. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 02. RCM No.: 2020-621.

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/s/

STEPHANIE L DEGRAW
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HINA S MEHTA
03/02/2021 02:36:52 PM

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:	November 19, 2020
To:	Courtney Hamilton, PharmD, BCPS Regulatory Project Manager **Division of Non-Malignant Hematology (DNH)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Susan Redwood, MPH, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Rebecca Falter, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI) and Instructions for Use (IFU)
Drug Name (established name):	STIMUFEND (pegfilgrastim-xxxx)[1]
Dosage Form and Route:	injection, for subcutaneous use
Application Type/Number:	BLA 761173
Applicant:	Fresenius Kabi USA, LLC

[1] STIMUFEND has been developed as a biosimilar to US-licensed pegfilgrastim. The proprietary name STIMUFEND was conditionally approved on June 19, 2020. At the time of this review, the non-proprietary name has not yet been determined; therefore, we use pegfilgrastim-xxxx as a placeholder until such time as it has been determined.

1 INTRODUCTION

On March 27, 2020, Fresenius Kabi USA, LLC submitted for the Agency's review an original Biologics License Application (BLA) 761173 for STIMUFEND (pegfilgrastim-xxxx) injection. The proposed indication for STIMUFEND (pegfilgrastim-xxxx) is to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia . This original BLA is a proposed biosimilar to Neulasta (pegfilgrastim), injection, for subcutaneous use BLA 125031.

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 Non-Malignant Hematology (DNH) on April 6, 2020, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for STIMUFEND (pegfilgrastim-xxxx) injection, for subcutaneous use.

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 STIMUFEND (pegfilgrastim-xxxx) injection PPI and IFU received on March 27, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 13, 2020.
- Draft STIMUFEND (pegfilgrastim-xxxx) Prescribing Information (PI) received on March 27, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 13, 2020.
- Approved Neulasta (pegfilgrastim) injection, for subcutaneous use, BLA 125031 labeling dated January 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.

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 PPI and IFU document using the Arial font, size 10.

In our collaborative review of the PPI and IFU we:

- simplified wording and clarified concepts where possible

- ensured that the PPI and IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI and IFU are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI and IFU meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI and IFU are consistent with the approved labeling where applicable.

4 CONCLUSIONS

The PPI 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 PPI and IFU are 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 PPI and IFU.

Please let us know if you have any questions.

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/s/

SUSAN W REDWOOD
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REBECCA A FALTER
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BARBARA A FULLER
11/19/2020 12:13:19 PM

LASHAWN M GRIFFITHS
11/19/2020 02:22:14 PM

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	November 2, 2020
Requesting Office or Division:	Division of Nonmalignant Hematology (DNH)
Application Type and Number:	BLA 761173
Product Name, Dosage Form, and Strength:	Stimufend [MSB11455]* (pegfilgrastim-xxxx)** Injection 6 mg/0.6 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Fresenius Kabi
FDA Received Date:	March 27, 2020, October 1, 2020, and October 26, 2020
OSE RCM #:	2020-621
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD
Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD

*MSB11455 has been developed as a proposed biosimilar to US-licensed Neulasta (pegfilgrastim). The proprietary name, Stimufend, is conditionally approved only with the approval of "MSB11455".

**The nonproprietary name for this BLA has not yet been determined; therefore, the placeholder, pegfilgrastim-xxxx, is used throughout this review to refer to the nonproprietary name for this product.

Reference ID: 4696032

1. REASON FOR REVIEW

Fresenius Kabi submitted 351(k) BLA 761173 on March 27, 2020 seeking licensure for Stimufend (pegfilgrastim-xxxx) as a biosimilar to US-licensed Neulasta. This review evaluates the proposed container label, carton labeling, Prescribing Information (PI), Patient Information, and Instructions for Use (IFU) for Stimufend for areas of vulnerability that could lead to medication errors.

1.1 PRODUCT BACKGROUND

US-licensed Neulasta (pegfilgrastim) was approved on January 31, 2002, under BLA 125031. Stimufend is being proposed for the indication of decreasing the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Stimufend is being proposed as a 6 mg/0.6 mL solution in a single-dose, ungraduated prefilled syringe with a passive needle guard. Like US-licensed Neulasta, Stimufend's syringe does not bear graduation marks and is intended only to deliver the entire contents of the syringe for direct administration.

1.2 REGULATORY HISTORY

On January 31, 2017, a BPD Type 2 meeting was held with the Sponsor (b) (4) During this meeting the Agency recommended that the Sponsor submit a comprehensive use-related risk analysis (URRA) for the proposed product to determine the necessity of a human factors (HF) validation study.[a]

On February 14, 2018, the Sponsor (b) (4) submitted their URRA under IND 113717. DMEPA evaluated the URRA, physical comparison, and IFU comparison of the proposed product (referred to as (b) (4) with US-licensed Neulasta. The review concluded that an HF validation study did not need to be submitted for Agency review for the proposed single-dose prefilled syringe at that time.[b]

As of June 24, 2019, the Sponsor for IND 113717 and BLA 761173 is Fresenius Kabi and the product code name is "MSB11455".

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

[a] Memorandum of Meeting Minutes for for (b) (4) (IND 113717). Silver Spring (MD): FDA, CDER, OHOP, DHP (US); 2017 JAN 31. https://darrts.fda.gov//darrts/faces/ViewDocument?documentId=090140af80429e8a&_afrRedirect=494556776850442

[b] Garrison, N. (b) (4) (IND 113717) Use-Related Risk Analysis Review. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JUL 30. RCM No. 2018-388.

Reference ID: 4696032

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	Appendix Section (for Methods and Results)
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other – Information Requests	E
Labels and Labeling	F
Pediatric Considerations	G

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. OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We performed a risk assessment of the proposed container label, carton labeling, PI, patient information, and IFU for Stimufend to determine whether there are deficiencies that may lead to medication errors and other areas of improvement.

Our evaluation of the proposed patient information did not identify unique areas of vulnerability that may lead to medication errors; however, our review of the proposed Stimufend PI, IFU, container label, and carton labeling identified unique areas of vulnerability that may lead to medication errors. We provide recommendations for the PI and IFU below.

Our recommendations for the container label and carton labeling were sent to Fresenius Kabi via information request on September 17, 2020 (see Appendix E). On October 1, 2020, Fresenius Kabi submitted revised container label and carton labeling. We note that most recommendations were implemented, however Fresenius Kabi did not implement the recommendations on the container syringe label (i.e. inclusion of NDC and route of administration) due to space constraints. The revised container syringe label and tray label are acceptable from a medication error perspective. However, our evaluation of the revised carton labeling identified a trailing zero (i.e., 30.0) on the back panel. As such, we sent our recommendation for the revised carton labeling on October 19, 2020 (see Appendix E). On October 26, 2020, Fresenius Kabi submitted revised carton labeling. Our review of the revised carton labeling did not identify unique areas of vulnerability that may lead to medication errors. We note a place holder is present for the nonproprietary name on the carton and container labeling.

4. CONCLUSION & RECOMMENDATIONS

Our evaluation of the proposed patient information did not identify unique areas of vulnerability that may lead to medication errors. We have no recommendations for the patient information at this time.

Our evaluation of the proposed Stimufend PI and IFU identified unique areas of vulnerability that may lead to medication errors. We provide recommendations for the division in Section 4.1 below. We advise they be implemented prior to approval of BLA 761173.

Our evaluation of the revised container label and tray label submitted on October 1, 2020 and carton labeling submitted on October 26, 2020 did not identify unique areas of vulnerability that may lead to medication errors. We have no further recommendations for the container label, tray label, and carton labeling at this time; however, we ask the Applicant to submit the updated container label and carton labeling once the nonproprietary name has been determined in Section 4.2 below.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. Prescribing Information
    1. Dosage Forms and Strengths [Highlights and Section 3]
        a. We recommend adding "for manual use only" to the end of the dosage form statement.

    2. How Supplied/Storage and Handling [16]
        a. As currently presented, the NDC is represented by a placeholder. We recommend requesting the proposed NDC for review.

B. Instructions for Use
    1. We recommend creating a "Guide to Parts" section as the first section of the IFU. Move Figure A and Figure B, which show the syringe before and after use, to the Guide to Parts section.

    2. We recommend renaming Figure A as "Before Use" and Figure B as "After Use".

    3. We recommend labeling the "finger grips" and "expiration date" on Figure A.

    4. We recommend adding the statement "Important: The needle is covered by a needle cap before use" under the Guide to Parts figures.

    5. We recommend revising [redacted] (b) (4) to read "Keep the pre-filled syringe in the original carton to protect from light or physical damage".

    6. Under the "Using the prefilled syringe" heading, we recommend adding two bullet points after the first bullet point that read:

        • Make sure the name STIMUFEND appears on the carton and prefilled syringe label.

        • Check the carton and prefilled syringe label to make sure the dose strength is 6 mg/0.6 mL.

Reference ID: 4696032

7. Under the "**Using the prefilled syringe**" heading, we recommend adding a statement warning users not to use a prefilled syringe if the needle guard is activated (2nd to last bullet point). For example, revise as follows:

(b) (4)

- **Do not** use a prefilled syringe if the needle guard has been activated. Use another prefilled syringe that has not been activated and is ready to use.

8. We recommend adding "adhesive bandage" as an item that should be gathered under the "**Prepare** (b) (4) heading. (b) (4)

9. We recommend removing the subheading (b) (4)

10. We recommend revising (b) (4)
For example, revise as follows:

(b) (4)

11. We recommend labeling Figures M and N with the appropriate injection sites to correspond with the text provided.

12. We recommend revising the statement (b) (4) to "thigh" in alignment with the US licensed Neulasta IFU.

13. We recommend deleting the statement (b) (4) as this information is redundant.

14. We recommend deleting (b) (4)

(b) (4)

15. We recommend adding the following statement to the end of the "**Choose an injection site**" section: "Choose a different injection site each time you give yourself an injection. If you want to use the same injection site, make sure it is not the same spot on the injection site you used for a previous injection."

16. Under the [redacted] (b) (4) heading, the image used in Figure P does not match the accompanying text. [redacted] (b) (4)

17. Under the [redacted] (b) (4) section, we recommend including additional warning statements [redacted] (b) (4) For example, revise as follows:

Do not remove the needle cap from the prefilled syringe until you are ready to inject.

Do not twist or bend the needle cap.

Do not hold the prefilled syringe by the plunger rod.

Do not put the needle cap back onto the prefilled syringe.

[redacted] (b) (4)

18. We recommend revising the [redacted] (b) (4) language to read [redacted] (b) (4)

19. We recommend deleting the statement [redacted] (b) (4)

20. We recommend relocating the statements "Do not try to recap the needle as it could lead to a needle stick injury.", [redacted] (b) (4)

21. We recommend revising the "**Important**" statement and bullet points to read "**Important:** When you remove the syringe, if it looks like the medicine is still in the syringe, this means you have not received a full dose. Call your healthcare provider right away." Additionally, the [redacted] (b) (4) statement may be deleted.

4.2 RECOMMENDATIONS FOR FRESENIUS KABI

Comments for the Container Label and Carton Labeling

1. We note the nonproprietary name for this BLA has not yet been determined; therefore, the placeholder, pegfilgrastim-xxxx, is used throughout the carton and container labeling. We recommend you submit updated carton and container labeling once the nonproprietary name has been determined.

Reference ID: 4696032

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for Stimufend that Fresenius Kabi submitted on March 27, 2020, and US-licensed Neulasta.

Table 2. Relevant Product Information for US-Licensed Neulasta and Stimufend

Product Name	US-licensed Neulasta[c]	Stimufend
Initial Approval Date	January 31, 2002	N/A
Proper or Nonproprietary Name	Pegfilgrastim	Pegfilgrastim-xxxx
Indication	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. Neulasta is also indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.	To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.
Route of Administration	Subcutaneous	Subcutaneous
Dosage Form	Injection	Injection
Strength	6 mg/0.6 mL	6 mg/0.6 mL
Dose and Frequency	Patients with cancer receiving myelosuppressive chemotherapy: • 6 mg administered subcutaneously once per chemotherapy cycle. • Do not administer between 14 days before and 24 hours after cytotoxic chemotherapy. • Use weight-based dosing for pediatric patients weighing less than 45 kg; refer to Table 1.	Patients with cancer receiving myelosuppressive chemotherapy: • 6 mg administered subcutaneously once per chemotherapy cycle. • Do not administer between 14 days before and 24 hours after cytotoxic chemotherapy. • Use weight-based dosing for pediatric patients weighing less than 45 kg; refer to Table 1.

[c] Neulasta [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. [cited 2020 AUG 06]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125031s199lbl.pdf.

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<tr>
<td></td>
<td>Patients with Hematopoietic Subsyndrome of Acute Radiation Syndrome:
• Two doses, 6 mg each, administered subcutaneously one week apart. Use weight-based dosing for pediatric patients weighing less than 45 kg; refer to Table 1.

The US-Neulasta prefilled syringe is not designed to allow for direct administration of doses less than 0.6 mL (6 mg). The syringe does not bear graduation marks, which are necessary to accurately measure doses of US-Neulasta less than 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of less than 0.6 mL (6 mg) is not recommended due to the potential for dosing errors. Refer to Table 1.

Table 1. Dosing of Neulasta for pediatric patients weighing less than 45 kg
<table>
<tr><th>Body weight</th><th>Neulasta Dose</th><th>Volume to administer</th></tr>
<tr><td>Less than 10kg*</td><td>See below*</td><td>See below*</td></tr>
<tr><td>10-20 kg</td><td>1.5 mg</td><td>0.15 mL</td></tr>
<tr><td>21-30 kg</td><td>2.5 mg</td><td>0.25 mL</td></tr>
<tr><td>31-44 kg</td><td>4 mg</td><td>0.4 mL</td></tr>
</table>
*For pediatric patients weighing less than 10 kg, administer 0.1 mg/kg (0.01 mL/kg) of US-Neulasta.</td>
<td>The Stimufend prefilled syringe is not designed to allow for direct administration of doses less than 0.6 mL (6 mg). The syringe does not bear graduation marks, which are necessary to accurately measure doses of Stimufend less than 0.6 mL (6 mg) for direct administration to patients. Thus, the direct administration to patients requiring dosing of less than 0.6 mL (6 mg) is not recommended due to the potential for dosing errors. Refer to Table 1.

Table 1. Dosing of Stimufend for Pediatric Patients Weighing Less than 45 kg
<table>
<tr><th>Body weight</th><th>Stimufend Dose</th><th>Volume to administer</th></tr>
<tr><td>Less than 10kg*</td><td>See below*</td><td>See below*</td></tr>
<tr><td>10-20 kg</td><td>1.5 mg</td><td>0.15 mL</td></tr>
<tr><td>21-30 kg</td><td>2.5 mg</td><td>0.25 mL</td></tr>
<tr><td>31-44 kg</td><td>4 mg</td><td>0.4 mL</td></tr>
</table>
* For pediatric patients weighing less than 10 kg, administer 0.1 mg/kg (0.01 mL/kg) of Stimufend.</td>
</tr>
<tr>
<td>How Supplied</td>
<td>US-Neulasta is a clear, colorless, preservative-free solution available as single dose prefilled syringe with an UltraSafe® Needle Guard, containing 6 mg/0.6 mL of pegfilgrastim as well as an OnPro kit which contains 6 mg/0.6 mL solution in a single prefilled syringe co-</td>
<td>Stimufend (pegfilgrastim-xxxx) injection is a sterile, clear, colorless, preservative-free solution supplied in a prefilled single-dose syringe for manual use containing 6 mg pegfilgrastim-xxxx, supplied with a 27-gauge ½-inch needle with a Safe’n’Sound® passive Needle Guard.</td>
</tr>
</table>

	packaged with the on-body Injector for US-Neulasta.	
Storage	Store refrigerated between 2° to 8°C (36° to 46°F) in the carton to protect from light. Do not shake. Discard syringes stored at room temperature for more than 48 hours. Avoid freezing; if frozen, thaw in the refrigerator before administration. Discard syringe if frozen more than once.	Store refrigerated between 36°F to 46°F (2°C to 8°C) in the carton to protect from light. Do not shake. Discard syringes stored at room temperature for more than 72 hours. Do not freeze. Discard syringe if frozen.

Reference ID: 4696032

APPENDIX B. PREVIOUS DMEPA REVIEWS

On August 6, 2020, we searched for previous DMEPA reviews relevant to this current review using the terms, 'IND 113717' and 'BLA 761173. Our search identified one previous review[d], and we considered our previous recommendations to see if they are applicable for this current review.

APPENDIX E. INFORMATION REQUESTS

Container Label and Carton Labeling Comments Sent to the Sponsor[e]

On September 17, 2020, the Agency issued an information request that included the following DMEPA recommendations for the container label and carton labeling.

RECOMMENDATIONS FOR FRESENIUS KABI

A. Container (Syringe) Label
    1. As currently presented, the inclusion of an NDC number is not indicated. We request you provide your proposed NDC and location for the NDC on the label for review.

    2. We recommend adding the route of administration "For subcutaneous use only" on the principal display panel as space allows.

B. Carton Labeling (Blister Tray)
    1. We note the use of a placeholder for the NDC (i.e., 63323-0000-0). We request you submit your proposed NDC for review.

    2. As currently presented the location of the lot and expiration date are not described. We recommend including the lot and expiration date on the blister tray to be in alignment with the outer carton labeling.

    3. We recommend adding the following information to the blister tray to be in alignment with the outer carton labeling:
        - Pegylated Recombinant Methionyl Human Granulocyte Colony-Stimulating Factor (PEG-r-metHuG-CSF) derived from E. coli
        - Sterile Solution – No Preservative

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[d] Garrison, N. (b) (4) (IND 113717) Use-Related Risk Analysis Review. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2018 JUL 30. RCM No. 2018-388.
[e] Hamilton, C. Information Request. 2020 SEP 17. Available at: https://darrts.fda.gov//darrts/faces/ViewDocument?documentId=090140af805973fa&_afrRedirect=1113007007543282

4. We recommend you revise [redacted] (b) (4) to include the full storage information as presented on the outer carton labeling (i.e., Store refrigerated between 36° to 46°F (2° to 8°C). Do not freeze or shake. Protect from Light).

C. Carton Labeling (Outer Carton)

1. We note the use of a placeholder for the NDC (i.e., 63323-0000-0). We request you submit your proposed NDC for review.

2. As currently presented, the inclusion of a linear barcode is not indicated. The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature that should be part of the label whenever possible. Therefore, we request you add the product's linear barcode to each carton as required per 21CFR 201.25(c)(2).

3. We note the inclusion of human-readable product identifier information; however, the inclusion of a machine-readable (2D data matrix barcode) product identifier is not indicated. Per the FDA draft guidance on product identifiers, ensure the panel containing the product identifier will also include a 2D data matrix barcode.[f]

4. Revise [redacted] (b) (4) to read "Dosage: See Prescribing Information" to ensure consistency with all doses described in the prescribing information.

Response: October 1, 2020, the Sponsor submitted revised container label and carton labeling.[g] See Appendix F.

[f] The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf

[g] Shobana, N. Fresenius Kabi Response to Information Request. Dated 2020 OCT 1. Available at: \\CDSESUB1\evsprod\bla761173\0014\m1\us\111-info-amend\response-to-information-request-ir12-dated-september-17-2020.pdf

Container Label and Carton Labeling Comments Sent to the Sponsor[h]

On October 19, 2020, the Agency issued an information request that included the following DMEPA recommendations for the carton labeling.

Carton Labeling (Outer Carton)

- We recommend removing the trailing zero from "30.0" that appears on the back panel to avoid a ten-fold misinterpretation of the number (i.e., 30.0 versus 300).

Response: October 26, 2020, the Sponsor submitted revised container label and carton labeling.[i] See Appendix F.

[h] Hamilton, C. Information Request. 2020 OCT 19. Available at: https://darrts.fda.gov//darrts/faces/ViewDocument?documentId=090140af805a10aa&_afrRedirect=2048043223959954

[i] Shobana, N. Fresenius Kabi Response to Information Request. Dated 2020 OCT 21. Available at: \\CDSESUB1\evsprod\bla761173\0018\m1\us\12-cover-letter\cover-letter.pdf

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,[j] along with postmarket medication error data, we reviewed the following Stimufend labels and labeling submitted by Fresenius Kabi on March 27, 2020.

- Container Label
- Container Label – Side by Side with US-licensed Neulasta (image not shown)
  \\cdsesub1\evsprod\bla761173\0001\m1\us\114-labeling\114a-draft-label\side-by-side-container-labeling-syringe.pdf
- Carton labeling
- Carton Labeling – Side by Side with US-licensed Neulasta (image not shown)
  \\cdsesub1\evsprod\bla761173\0001\m1\us\114-labeling\114a-draft-label\side-by-side-container-labeling-blister.pdf
  \\cdsesub1\evsprod\bla761173\0001\m1\us\114-labeling\114a-draft-label\side-by-side-container-labeling-carton.pdf
- Prescribing Information – includes Instructions for Use (image not shown)
  \\CDSESUB1\evsprod\bla761173\0001\m1\us\114-labeling\114a-draft-label\labeling-contingency-000045465.doc
- Prescribing Information – Side by Side with US-licensed Neulasta (image not shown)
  \\CDSESUB1\evsprod\bla761173\0001\m1\us\114-labeling\114a-draft-label\labeling-contingency-000045462.pdf

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

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APPENDIX G. Pediatric Considerations

As part of Fresenius Kabi's submission to BLA 761173, Frensenius Kabi submitted a request for deferral for its pediatric assessments. We note the following:

- October 4, 2019, DMEPA memorandum (archived to BLA 125031). On October 4, 2019, DMEPA finalized a memorandum of a comprehensive review and analysis of medication errors associated with doses of pegfilgrastim products less than 0.6 mL (6 mg) in pediatric patients. Stimufend has the same strength, dosage form, and route of administration as US-licensed Neulasta, and, like US-licensed Neulasta, would only be available in a prefilled syringe without graduation marks. Additionally, the proposed labeling for Stimufend, in relevant part, is substantially the same as US-licensed Neulasta's labeling, including with respect to pediatric use information and the statements that the prefilled syringe is not designed to allow for direct administration and cannot accurately measure doses less than 0.6 mL (6 mg). Therefore, if the requirements for biosimilarity are met, Stimufend would be expected to be associated with the same type of dosing error and potential consequences as US-licensed Neulasta. See also October 10, 2019, Memorandum on Requirements for Pediatric Assessments Pursuant to Section 505B(b)(1) of the FD&C Act.
- Order letter to sponsor of US-licensed Neulasta. On October 10, 2019, FDA issued an order letter pursuant to section 505B(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) to the sponsor of US-licensed Neulasta, requiring it to submit pediatric assessments as described in section 505B(a)(2)(A) of the FD&C Act. As described in the letter, the sponsor of U.S.-licensed Neulasta is subject to a postmarketing requirement referred to as submission of pediatric assessments for Neulasta (pegfilgrastim) as described in section 505B(a)(2)(A) of the FD&C Act, including development of an "appropriate formulation" (presentation) that can be used to directly and accurately administer Neulasta (pegfilgrastim) to pediatric patients who weigh less than 45 kg and require doses that are less than 0.6 mL (6 mg), and conducting any necessary human factors studies to evaluate the ability of healthcare providers and/or caregivers to measure the appropriate doses. In the letter, FDA stated it expected that a pediatric presentation – such as a vial or a pediatric-sized pre-filled syringe (with an appropriate concentration of product) – that can be used to directly and accurately deliver doses of less than 0.6 mL (6 mg) of pegfilgrastim to pediatric patients could be an "appropriate formulation" as described in section 505B(a)(2)(A). NON-RESPONSIVE

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

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

Memorandum

Date: October 20, 2020

To: Courtney Hamilton, PharmD, BCPS, Regulatory Project Manager, Division of Nonmalignant Hematology (DNH)

Virginia Kwitkowski, MS, ACNP-BC, Associate Director for Labeling, (DNH)

From: Rebecca Falter, PharmD, BCACP, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Susannah O'Donnell, MPH, RAC, Team Leader, OPDP

Subject: OPDP Labeling Comments for Stimufend (pegfilgrastim-xxxx) injection, for subcutaneous use

BLA: 761173

In response to DNH's consult request dated April 6, 2020, OPDP has reviewed the proposed product labeling (PI), Instructions for Use (IFU), and carton and container labeling for the original BLA submission for Stimufend. Per communications by electronic mail with Courtney Hamilton on October 15, 2020, OPDP has reviewed the proposed patient package insert (PPI) as well.

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling received by electronic mail from DNH (Courtney Hamilton) on October 13, 2020, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI and IFU will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on October 1, 2020, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Rebecca Falter at (301) 837-7107 or Rebecca.Falter@fda.hhs.gov.

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CLINICAL INSPECTION SUMMARY

Date	October 19, 2020
From	Anthony Orencia M.D., F.A.C.P., Medical Officer Min Lu, M.D., M.P.H., Team Leader Kassa Ayalew, M.D., M.P.H., Branch Chief Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Julie Weisman, M.D., Medical Officer Tanya Wroblewski, M.D., Medical Team Leader Ann Farrell, M.D., Director Courtney Hamilton, PharmD., BCPS Lattice Wilson, Regulatory Project Manager Charlene Wheeler, Acting Chief Project Manager Division of Nonmalignant Hematology (DNH)
BLA	761173
Applicant	Fresenius Kabi SwissBiosim GmbH
Drug	Stimufend™ (MSB11455, pegylated granulocyte colony-stimulating factor), proposed biosimilar to Neulasta®
NME	Yes
Division Classification	Pegylated granulocyte colony-stimulating factor
Proposed Indication	Treatment of adult patients with febrile neutropenia
CDER Memo Issuance Date	June 2, 2020
Summary Goal Date	Original: October 5, 2020 (Extended: October 30, 2020)
Action Goal Date	March 1, 2021
BsUFA Date	March 27, 2021

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Two studies (EMR200621-001 [PK/PD] and EMR200621-003 [immunogenicity and safety] were submitted in support of BLA 761173 for the drug MSB11455 (Stimufend™), a pegylated granulocyte colony stimulating factor, proposed biosimilar to Neulasta®. The review division requested a sponsor inspection to evaluate the sponsor's oversight and quality control for these two studies.

At the current time, the COVID-19 global pandemic has significantly limited our ability to conduct on-site GCP investigations. As a result, a remote assessment was conducted for the sponsor using a WebEx platform for meetings, and review of original records that were uploaded to a secure box account licensed to the FDA for the investigation.

Sponsor remote investigation conducted by FDA to assess clinical trial oversight adequacy, site procedures, record keeping and reporting procedures regarding patient eligibility, adverse event reporting, and assessment of protocol deviations did not demonstrate any significant deficiencies.

The Fresenius Kabi SwissBiosim GmbH remote site investigation did not identify regulatory findings with sponsor oversight of these two clinical studies. Sponsor's conduct for clinical trials EMR200621-001 and EMR200621-003 appeared acceptable.

II. BACKGROUND

MSB11455, a pegylated granulocyte colony stimulating factor (G-CSF), is a proposed biosimilar to the reference product Neulasta® (pegfilgrastim). The proposed therapeutic indications and dosing regimen for MSB11455 are the same as for Neulasta®.

The sponsor proposes the biosimilar MSB11455 (tradename Stimufend™) as a leukocyte growth factor indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Two studies, Studies EMR200621-001 and EMR200621-003, form the basis for the regulatory decision-making process for this application.

Study EMR200621-001:

Study EMR200621-001 was a Phase I randomized, double-blind, crossover study to show equivalence between the pharmacokinetic (PK) and pharmacodynamic (PD) profile of MSB11455 and US-licensed Neulasta® in adult healthy subjects.

Subjects received either MSB11455 or Neulasta® on Day 1 of Period 1. After a washout period of 42 days, subjects who received MSB11455 in Period 1 were to receive Neulasta® on Day 1 of Period 2 and subjects who received Neulasta® in Period 1 were to receive MSB11455 on Day 1 of Period 2.

Study EMR200621-001 was conducted at two study sites in Australia. The study was conducted from August 2017 to May 2018. An interim analysis was planned after 276 randomized subjects (information fraction 80%) corresponding to 234 evaluable subjects. The last subject's last visit for the interim cut-off was May 8, 2018.

An Independent Data Monitoring Committee (IDMC) reviewed the Phase I data, including primary endpoints. In addition, the Sponsor performed an ongoing blinded safety data review throughout the study.

Study EMR200621-003:
Study EMR200621-003 was a Phase I randomized, double-blind, parallel group, controlled study to compare the immunogenicity and safety of MSB11455 and US-licensed Neulasta® in adult healthy subjects.

Each subject received two study drug administrations of either MSB11455 or Neulasta®. Period 1 started with the randomization of the subjects to one of the 2 treatment arms. Subjects received either MSB11455 or Neulasta® on Day 1 of Period 1. After a washout period of 28 to 35 days, subjects received the same study drug on Day 1 of Period 2.
Study EMR200621-003 was conducted at two study sites in New Zealand. The study was conducted from August 2017 to May 2018. At the time of the cut-off for the interim analysis, 336 subjects had been randomized. The last subject last visit for the unblinded interim cut-off was May 3, 2018.

An Independent Data Monitoring Committee reviewed the Phase I data, including primary endpoints. The Sponsor performed an ongoing blinded safety data review throughout the study.

III. RESULTS

Fresenius Kabi SwissBiosim GmbH
Terre Bonne Business Park
Route de Crassier 23/Bâtiment A3
1262 Eysins, Switzerland

Sponsor remote site assessment dates: August 10 to 19, 2020

Fresenius Kabi SwissBiosim GmbH is located in Terre Bonne Business Park, Eysins, Switzerland.

(b) (4) was the initial sponsor of the clinical research activities in IND 113717. The first subject in Study EMR200261-001 was enrolled on August 23, 2017 and the first subject in study EMR200621-300 was enrolled on August 21, 2017. The continuing application sponsor, Fresenius Kabi, acquired the clinical research activities in IND 113717, which included studies EMR 200621-001 and EMR 200621-003 on August 31, 2017.

The protocols for Studies EMR200261-001 and EMR200261-003 were developed and written by (b) (4) had oversight of protocol development. (b) (4) was also responsible for the selection of the clinical investigators, for signing the Form FDA 1572 (statement of the investigator form), and for completion of the required financial disclosure documents.

(b) (4) perform the data analyses for the studies. The data management plan, monitoring and review of adverse events and serious adverse events were contracted to (b) (4) for the following activities: drug accountability at the study site; project management and administration, investigational site monitoring; medical oversight and review; data management; statistical analysis; medical and statistical report writing.

An overview of the current BLA applicant Fresenius' responsibilities involved the following sponsor activities: clinical trial set-up activities; provision of clinical trial drug supplies; drug safety evaluation and SAE reporting; clinical site audits and other quality assurance audits; and

mandatory clinical trial website publications; laboratory logistics and management; review of organizational charts; transfer of obligations; investigator agreements; ethics board reviews and other approvals.

No discrepancies in the monitoring visits were observed.

No underreporting of serious adverse events was observed.

No significant regulatory deficiencies were observed during the remote site investigation. Sponsor appeared to conduct adequate oversight of the clinical studies under its purview. The remote site investigation did not reveal any significant data integrity issues.

{See appended electronic signature page}
Anthony Orencia, M.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}
Min Lu, M.D., M.P.H.
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Office of Scientific Investigations

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Division of Hematology Products Associate Director for Labeling Review of the Prescribing Information

Product Title	STIMUFEND® (pegfilgrastim-xxxx) injection, for subcutaneous use
Applicant	Fresenius Kabi
Application/Supplement Number	BLA 761173
Is Proposed Labeling in Old Format? (Y/N)	N
Is Labeling Being Converted to PLR? (Y/N)	N
Is Labeling Being Converted to PLLR? (Y/N)	N
Approved Indication(s)	n/a
Date FDA Received Application	03/27/2020
Review Classification (Priority/Standard)	S
Action Goal Date	03/26/2020
Review Date	09/17/2020
Reviewer	Virginia Kwitkowski, MS, ACNP-BC

This Associate Director for Labeling (ADL) review provides recommendations on the content and format of the Warnings and Precautions section of the prescribing information (PI) to help ensure that PI:

- Is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) requirements[1]
- Is consistent with labeling guidance recommendations[3] and with CDER/OND best labeling practices and policies
- Conveys the essential scientific information needed for safe and effective use of the product
- Is clinically meaningful and scientifically accurate
- Is a useful communication tool for health care providers
- Is consistent with other PI with the same active moiety, drug class, or similar indication

Background:
Fresenius Kabi has submitted a proposed biosimilar to Neulasta (pegfilgrastim).

Reviewer Comments: I have reviewed the draft labeling by comparing it to the labeling for reference product (Neulasta) as well as the most recently approved biosimilar to Neulasta, Nyvepria. Overall, the labeling was nearly identical to the currently approved Neulasta labeling; however, I do have some recommended edits to suggest to be consistent with the Biosimilar Labeling Guidance and recently approved biosimilar, Nyvepria.

[1] See *January 2006 Physician Labeling Rule*; 21 CFR 201.56 and 201.57; and *December 2014 Pregnancy and Lactation Labeling Rule* (the PLLR amended the PLR regulations). For applications with labeling in non-PLR "old" format, see 21 CFR 201.56(e) and 201.80.
[3] See *PLR Requirements for PI* website for PLR labeling guidances.

Attachments: Revised labeling with track changes edits and bubble comments explaining the revisions.

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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: 8/3/2020

TO: Division of Non-Malignant Hematology (DNH)
Office of Cardiology, Hematology, Endocrinology and Nephrology (OCHEN)

FROM: Division of New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

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

RE: BLA 761173

The Division of New Drug Study Integrity (DNDSI) within the Office of Study Integrity and Surveillance (OSIS) determined that inspections are not warranted at this time for the sites listed below. The rationale for this decision is noted below.

Rationale

Nucleus Network, Ltd.: The Office of Regulatory Affairs (ORA) inspected the clinical site in December 2017, which falls within the surveillance interval. The inspection was conducted under the following submission: NON-RESPONSIVE. The final classification for the inspections was No Action Indicated (NAI).

Q-Pharm Pvt., Ltd.: Although OSIS has no inspection history for the clinical site, recent and satisfactory inspection history exits for the Nucleaus Network clinical site that enrolled a significant number of total subjects (72%) in the current study and as such, the overall conduct for the study appears adequate.

(b) (4) OSIS inspected the analytical site in (b) (4), which falls within the surveillance interval. The inspection was conducted under the following submission: NON-RESPONSIVE. The final classification for the inspection was No Action Indicated (NAI).

Therefore, based on the rationale described above, inspections are not warranted at this time.

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	Nucleus Network, Ltd.	B The Centre for Clinical Studies, 5th Floor, Burnet Tower, AMREP Precinct, 89 Commercial Road, Melbourne, Victoria, Australia
Clinical	Q-Pharm Pvt., Ltd.	Level 5, Clive Berghofer Cancer Research Centre (CBCRC), 300C Herston Road, Herston, Brisbane, Queensland, Australia
Analytical	(b) (4)	

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