

Our Reference: BLA 125611/0

Novo Nordisk Inc.
Attention: Ms. Patricia D. Wilson
November 23, 2016
Sent by email

Dear Ms. Wilson:

We are reviewing your May 16, 2016 biologics license application for Coagulation Factor IX (Recombinant), GlycoPEGylated. We are providing the following comments and request for additional information to continue our review:

1. The information provided in the BLA regarding your column lifetimes studies for performance indicator parameters is not sufficient for us to understand how these studies are being conducted as you have not provided clear criteria that will be used to determine how the acceptability of re-use of the resins will be determined. Please provide the acceptance criteria and current results for the column lifetime studies for the columns used for the NONACOG BETA PEGOL (b) (4) manufacturing steps (b) (4) that support your ability to clean the (b) (4) as well as remove (b) (4).
2. Please clarify and describe if a study was performed to support that the NONACOG BETA PEGOL (b) (4) remains at temperature during shipping from your production facility in (b) (4) to the (b) (4), or provide a rationale for why such a study is not necessary.
3. Please clarify and describe if a study was performed to support that the NONACOG BETA PEGOL (b) (4) remains at temperature during shipping from the (b) (4) production facility to the Drug Product production facility in (b) (4), or provide a rationale for why such a study is not necessary.
4. Please clarify and describe if the container closure system used for the Histidine Solution co-packaged with NONACOG BETA PEGOL is identical to the one co-packaged with NOVOEIGHT or provide a description of any differences.
5. Please clarify if the microbiological and chemical quality control testing stated to be performed at the (b) (4) facilities in (b) (4) and (b) (4) is release testing for the Histidine Solution in the final container or in-process testing.

6. Please provide the following information regarding the complete NONACOG BETA PEGOL combination product including the vialled drug product, diluent in a prefilled syringe and vial adaptor:
 - a. The design history file
 - b. The summative usability test for (b) (4) (document UT84)
 - c. A summary of how you comply with the requirements for design controls under 21 CFR 820.30 (for the combination product and for each device and device component)
 - d. A summary of how you comply with the requirements for purchasing controls under 21 CFR 820.50 (for the combination product and for each device and device component)
 - e. A summary of how you comply with the requirements for corrective and preventative action under 21 CFR 820.100 (for the combination product and for each device and device component)
7. Please provide the limits for the microbial environmental monitoring program in the classified manufacturing areas in Building (b) (4) used to manufacture the NONACOG BETA PEGOL Drug Substance.
8. Please provide a summary of how the rooms in Building (b) (4) used to manufacture the NONACOG BETA PEGOL Drug Substance are cleaned. Please also clarify if disinfectant effectiveness studies covering the materials of construction in these manufacturing areas have been performed. Please provide a brief summary of these studies if they were performed or a rationale for why they are not necessary if they were not conducted.
9. Please provide a summary description of the environmental monitoring performance qualification performed to qualify the HVAC system and classified rooms in Building (b) (4) used to manufacture NONACOG BETA PEGOL.
10. Please clarify how the initial cleaning validation for the (b) (4) bioreactor used for manufacturing (b) (4) was performed so that it was under worst-case conditions compared to routine production which can include up to (b) (4) of continuous cultivation in this bioreactor.

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

Please submit your response and your notification of the shipment for this request as an amendment to this file by December 7, 2016 referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW
If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us at the above address by mail.
Thank you

If we determine that your response to this information request constitutes a major amendment, we will notify you in writing.

The action due date for this file is June 3, 2017.

Please send an acknowledgement message for receipt of this request.

If you have any questions, please contact me at (240) 402-8443.

Sincerely,
Edward Thompson
Regulatory Project Manager
FDA/CBER/OTAT/DRPM