



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

Our Reference: STN 125611/0

Novo Nordisk Inc.
Attention: Ms. Patricia D. Wilson
July 19, 2016
Sent by email

Dear Ms. Wilson:

We are reviewing your May 16, 2016 biologics license application for Coagulation Factor IX (Recombinant), GlycoPEGylated. We determined that the following information is necessary to continue our review:

Bioburden for (b) (4)

1. CBER finds bioburden qualification report (ID 002326607) incomplete since it does not include evaluation of (b) (4) in accordance with (b) (4). CBER requests (b) (4) evaluation of (b) (4) be completed and submitted for continued review.
2. Please provide back titration results for positive control used in bioburden qualification report (ID 002326607) for (b) (4). In addition, please provide results of negative control performed during the qualification study.
3. Bioburden specification of (b) (4) seems very high when your process capability has shown (b) (4) for the lots reported under Section 3.2.S.4.4, Batch Analysis. CBER requests the reevaluation of your specification so it better reflects your production process capabilities to provide better quality control oversight of the manufacturing process; or the setting of an alert limit to satisfy this requirement.

Sterility for Drug Product (DP)

4. Please provide back titration results for positive control used in qualification study of sterility test (report 002326602). In addition, please provide results of negative control performed during the qualification study.

Endotoxin for (b) (4) DP

5. Endotoxin inhibition/enhancement testing for (b) (4) DP (report 002328225) reported the selection of testing dilutions of (b) (4), respectively. CBER would like to know if other testing dilutions were tested to determine the optimal positive product control (PPC) spike recovery? If so, CBER would like to see these results supporting the selection of a (b) (4) DP testing dilution that provided average PPC % recoveries of (b) (4) which are on the higher end of the acceptable (b) (4) recovery range.
6. You DP endotoxin specification of (b) (4) is high when your process capability has shown results of (b) (4) for the lots reported under Section 3.2.P.5.4, Batch Analysis. CBER requests the reevaluation of this specification so it better reflects your production process capabilities to provide better quality control oversight of the manufacturing process; or the setting of an alert limit to satisfy this requirement.

Histidine Solution

7. Please provide sterility (b) (4) qualification reports for histidine solution as performed by (b) (4).

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 to this information request as an amendment to this file by August 2, 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.

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/OBRR