

Our Reference: BLA 125611/0

Novo Nordisk Inc.
Attention: Ms. Patricia D. Wilson
February 2, 2017
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:

Please reference your response submitted on November 14, 2016 and November 28, 2016 that have been designated as amendments 17 and 19 respectively:

Polysorbate 80 by (b) (4)
Method Validation:

1. You stated that using (b) (4) provided more accurate repeatability results than that from (b) (4) determinations. We do not agree that your results demonstrate repeatability. Please provide repeatability assessment results with either (b) (4) replicates of nominal concentration or (b) (4) different concentrations of Polysorbate 80 in nonacog beta pegol, using the experimental procedure you are validating, as was requested in our previous Information Request.
2. On page 15 of the method (b) (4) validation report document ID NovoDOCS 001870476 you assessed method robustness by varying (b) (4). You concluded that the tested parameters at high and low levels did not have any significant effect on the analytical procedure. Please provide data from each of the parameters at low and high levels, in comparison with those from the established (b) (4) method conditions in support of your conclusion.

Sucrose/Mannitol by (b) (4)

Method Validation

3. You stated that (b) (4) design which used (b) (4) provides a better estimate of repeatability of the method (b) (4) degrees of freedom. We do not agree that your results demonstrate repeatability. Please provide assessment results with either (b) (4) replicates of nominal concentration or (b) (4) different concentrations of Polysorbate 80 in nonacog beta pegol, using the experimental procedure you are validating, as was requested in our previous Information Request.
4. In section 5.6 of the validation of Analytical Procedure (b) (4) (Determination of sucrose and mannitol contents by (b) (4) , you stated that “The test parameters at high and low levels did not have any significant effect on the analytical results, except for temperature where the effect (max. (b) (4) was not considered to be critical.” Please provide experimental data to support the robustness assessment of the method (b) (4)
5. It is not clear to us what “...except for temperature where the effect (max. (b) (4)) was not considered to be critical” means. Please explain.

(b) (4) .

Method

6. In document novoDOCS 002255855 in module 3.2.P.5.3 Validation of Analytical Procedures, you stated that the analysis on nonacog beta pegol was performed in accordance with (b) (4) , with minor modifications. Please provide the standard operation procedure outlining these modifications.

Method Verification.

7. You listed a series of requirements for calibration of the (b) (4) solution that includes system suitability, repeatability (%RSD), mean of (b) (4) replicates standard (b) (4) etc. There are no data showing that your (b) (4) actual performance met these conditions. Please provide calibration data showing that the instrument performance met the modified criteria.
8. In your study design, you stated that “A double determination of the test sample was conducted in one analytical series”. Please submit your verification report using nonacog beta pegol drug product.

Determination of Particulate matter (b) (4)

Method Verification

9. Your study design shows that you use (b) (4) of drug product samples for the verification of the (b) (4) method (b) (4) “Determination of Particulate Matter”. Please submit your verification report for the method.

Determination of (b) (4)

Method Verification

10. (b) (4) was used for the determination of (b) (4) of nonacog beta pegol sample solutions. Please provide the method Verification report.

The review of this application is on-going and issues may be added, expanded upon, or modified.

Please submit your response and your notification of the shipment for this request as an amendment to this file by February 16, 2017, 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/OTAT/DRPM