



Our Reference: BLA 125611/0

Novo Nordisk Inc.
Attention: Ms. Patricia D. Wilson
September 12, 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:

We have reviewed the following assays and their method validations in your submission of the original BLA application, STN 125611, received on 16 May 2016.

Polysorbate 80 by (b) (4)

1. Method Validation: Precision-Repeatability.

On page 12 and 13 of the Validation of the Analytical Procedure (b) (4), you used (b) (4) design with (b) (4); however only (b) (4) replicate determinations were provided for each condition. Please provide data for repeatability with either (b) (4) replicate determinations at the nominal concentration or (b) (4) determinations each at (b) (4) different concentrations over the assay range.

Sucrose/Mannitol by (b) (4)

2. Method Validation

- a. Precision/Repeatability- On page 15 and 16 of the Validation of the Analytical Procedure (b) (4), you established repeatability based on (b) (4). However, for each condition (b) (4) you only provided (b) (4) determined values. Please provide data for repeatability with either (b) (4) replicate determinations at the nominal concentration or (b) (4) determinations each at (b) (4) different concentrations over the assay range.
- b. Accuracy- You stated on page 16, section 5.5 that the accuracy of the method was inferred from linearity, specificity and precision. Please provide analysis of your linearity, specificity and precision data to show how you inferred accuracy of the

method. Otherwise, please provide accuracy data minimally at three concentration level over the assay range, including concentrations below and above the nominal concentrations for both sucrose and mannitol.

- c. Range- You stated that the range for the method was determined on the basis of the linearity results. We do not agree. The range should be based on the assessment from linearity, accuracy, precision and specificity. Please reevaluate your data to determine range of your method based on linearity, accuracy, precision and specificity results and submit for review.

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 notification of the shipment for this request as an amendment to this file by September 30, 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