

Dehdashti, Seameen (Jean)

From: Dehdashti, Seameen (Jean)
Sent: Tuesday, December 04, 2018 12:00 PM
To: 'BDV (Barbara Davies)'
Cc: Dehdashti, Seameen (Jean)
Subject: FDA Information Request - CMC: BLA 125671/0

Dear Barbara,

We are reviewing your BLA submission for Antihemophilic Factor (Recombinant), GlycoPEGylated, turoctocog alfa pegol (STN 125671), and have the following information request (IR), outlined below in **bold text**. Please send us your response by close of business, Monday, December 31, 2018.

FDA Information Request (IR) – CMC:

1. Regarding the stability of the Primary Reference Material (PRM):

- a. Please investigate the increase in the potency of (b) (4) over time observed in the stability studies and assess its potential impact on the shelf-life of the current PRM, and potency assignment of the product.**
- b. Please provide the potency data for (b) (4) at all time-points from all the stability studies and a side-by-side comparison of the stability profiles of all the PRMs.**
- c. Please reanalyze the (b) (4) data for (b) (4) using the algorithm described in Section 3.2.S.3.1. Elucidation of Structure and provide the PEGylation profile for each sample tested in the stability studies.**
- d. To better monitor the stability of the PRM, please continue to use the (b) (4) as the reference standard and test all the Reference Materials (b) (4) at least (b) (4) a year.**
- e. We suggest lowering the long-term storage temperature of the PRM and *Secondary Reference Material* (SRM) to (b) (4).**

2. Please address the following discrepancies:

- a. In several places of the Summary of Section 3.2.S.5 *Establishment of Novo Nordisk Secondary Reference Material*, the turoctocog alfa pegol PRM batch is referred to as (b) (4), and the SRM batch is referred to as (b) (4).**
- b. There are also incorrect batch designations for the PRM and SRM in Section 3.2.S.5 *Establishment of Primary Reference Material*.**

Please confirm receipt of this communication, and do not hesitate to contact me, should you have any questions and/or concerns.

Warm regards,

Jean Dehdashti, MSc, RAC
Regulatory Project Manager

Center for Biologics and Evaluation
Office of Tissues and Advanced Therapies
U.S. Food and Drug Administration
Tel: 240-402-9146
Seameen.Dehdashti@fda.hhs.gov



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