

**From:** [Dehdashti, Seameen \(Jean\)](#)  
**To:** "BDV (Barbara Davies)"  
**Cc:** [Dehdashti, Seameen \(Jean\)](#)  
**Subject:** FDA Information Request (IR)-CMC: BLA 125671/0  
**Date:** Thursday, August 09, 2018 12:03:30 PM  
**Attachments:** [image003.png](#)  
**Importance:** High

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Good afternoon Barbara,

Reference is made to Novo Nordisk, Inc., original BLA 125671 submission, dated February 27, 2018. We are reviewing your BLA submission for Antihemophilic factor, GlycoPEGylated (STN125671) and have the following information request (IR), outlined in **bold text** below. Please provide your response by Friday, August 24, 2018.

**FDA CMC IR:**

- 1. With reference to the viral clearance studies on turoctocog alfa pegol (i.e., Antihemophilic Factor (Recombinant), GlycoPEGylated) in Section 3.2.A.2, please provide data to qualify that the down-scale systems used for the viral clearance validation studies are representative of the respective manufacturing steps at the proposed commercial-scale. The steps include Purification (b) (4), and Purification by (b) (4)**
- 2. With reference to the viral clearance studies on Anti-FVIII mAb in Section 3.2.A.2, please provide data to qualify that the down-scale systems used for the viral clearance validation studies are representative of the respective manufacturing steps at the proposed commercial-scale. The steps include (b) (4) 20N filtration.**
- 3. With reference to the viral clearance studies on (b) (4) in Section 3.2.A.2, please provide data to qualify that the down-scale systems used for the viral clearance validation studies are representative of the respective manufacturing steps at the proposed commercial-scale. The steps include (b) (4) Triton X-100 (b) (4) 20N filtration.**
- 4. In your viral clearance studies on turoctocog alfa pegol using the (b) (4) Purification by (b) (4), and Purification by (b) (4), you had (b) (4) for each tested virus. To demonstrate the effectiveness of the relevant viral clearance steps before they reach the life-cycle limit of each (b) (4), please have (b) (4) runs for each tested virus in these studies.**
- 5. In your viral clearance studies on turoctocog alfa pegol, please provide the data on cytotoxicity and interference to demonstrate that the components used in these assays do not adversely affect the (b) (4)**
- 6. In your viral clearance study #211207, each sample (b) (4)**

(b) (4), whereas in the similar viral clearance study #300058, each sample was not (b) (4). Please provide the data on cytotoxicity and interference to demonstrate that the components used in the viral clearance assays do not adversely affect the (b) (4)

7. In your viral clearance study #213193, each sample was (b) (4) whereas in the similar viral clearance study #300090, each sample (b) (4). Please provide the data on cytotoxicity and interference to demonstrate that the components used in the viral clearance assays do not adversely affect the (b) (4)
8. Please provide the complete method validation reports on the quantitative (b) (4) included in the relevant viral clearance studies.
9. Please confirm if the (b) (4) in the manufacture of anti-FVIII Mab can be (b) (4). If yes, please provide the viral clearance data to demonstrate the effectiveness of this step before the (b) (4) reaches its life-cycle limit.
10. Please confirm if the (b) (4). Triton X-100 (b) (4) in the manufacture of (b) (4). If yes, please provide the viral clearance data to demonstrate the effectiveness of these steps before the (b) (4) reach their life-cycle limits.

Please confirm receipt of my e-mail, and do not hesitate to contact me, should you have any questions and/or concerns.

Warm regards,

**Jean Dehdashti, MSc, RAC**  
**Regulatory Project Manager**

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