

Dehdashti, Seameen (Jean)

From: Dehdashti, Seameen (Jean)
Sent: Friday, October 12, 2018 3:15 PM
To: 'BDV (Barbara Davies)'
Cc: Dehdashti, Seameen (Jean)
Subject: FDA Information Request (IR): BLA 125671/0

Importance: High

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 Friday, October 26, 2018. If you feel that you will not be able to meet this timeline, please propose the date by which you can provide the requested data.

FDA Information Request (IR):

1. **Some Drug Substance (DS) specifications are not sufficiently justified. Your approach to justify the specifications based on (b) (4) is not always appropriate. Also, you included data from lots manufactured using the clinical processes to establish the acceptance criteria, when the commercial process has demonstrated significantly higher consistency for some parameters. To better control for manufacturing consistency, please revise the following acceptance criteria in the DS specifications by using a tighter statistical approach, i.e., no more than (b) (4), and excluding the data from the clinical lots in the calculation of the acceptance criteria because they are not representative of the commercial process, which has been much improved.**

a. (b) (4)



2. You did not provide data or detailed justifications to support most of the Drug Product (DP) specifications. Some DP acceptance criteria are established based on DS acceptance criteria with some data from DP manufacture. It is not clear how the specifications for XX and YY are determined, or if the actual test results are relevant to the proposed acceptance criteria. Please provide the data, and establish appropriately justified acceptance criteria for the following parameters in the DP specifications:
- a. **Reconstitution time/solubility:** No data and statistical justification were provided.
 - b. (b) (4)
 - f. **Purity:** No actual test was provided to demonstrate the capability of the manufacturing process to meet the acceptance criteria. The purity in the clinical lots was significantly higher than the proposed acceptance limit.
 - g. (b) (4)
 - h. **Polysorbate 80:** No data and statistical justification were provided.
 - i. **Bacterial endotoxins:** You did not provide results for the testing of endotoxins in the Drug Product. Please provide the data, and establish an appropriately justified action limit to allow for the control of manufacturing consistency.

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

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of Tissues and Advanced Therapies
U.S. Food and Drug Administration

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