

Dehdashti, Seameen (Jean)

From: Dehdashti, Seameen (Jean)
Sent: Monday, November 26, 2018 2:08 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 10, 2018.

FDA Information Request (IR) – CMC (Facility)

We reviewed your responses to our October 12, 2018 information request (IR), which were submitted on November 2, 2018 as Amendment 37 to the original BLA, and found your responses to the following questions to be inadequate.

1. Drug Substance specifications

1.e. (b) (4)

We acknowledge the revisions you made to the specification for the (b) (4). The adequacy of the revised specification will be determined when we review the revised analytical procedure and the associated validation report, which you have committed to submit by December 19, 2018.

2. Drug Product specifications

2.a. Reconstitution time/solubility

Your proposed acceptance criterion (b) (4) is based on a (b) (4), which is not a legally recognized (b) (4) in the United States. Also, the applicability of this acceptance criterion to a chemically modified protein, such as Esperoct, is not established. Since anomalies in reconstitution time can be indicative of issues encountered during Drug Product manufacture, this parameter needs to be well controlled to ensure manufacturing consistency. Please provide the actual reconstitution times for all manufactured lots, and establish a statistically justified acceptance criterion based on these data, or justify the use of the current acceptance criterion.

2.b (b) (4)

2.c (b) (4)

(b) (4)

2.d (b) (4)

2.f Purity

We disagree with your approach to establish the acceptance criterion for *Purity* of the Drug Product based on the acceptance criterion for the (b) (4) of the Drug Product manufacturing and handling processes. It is not clear how these (b) (4) were “estimated”, moreover, comparison of the data for the (b) (4)) and Drug Product (b) (4)) does not support the magnitude of these (b) (4) and validity of your model. Please justify and establish the acceptance criterion for *Purity* of the Drug Product based on statistical analysis of release testing data.

2.g (b) (4)

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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