

From: Maruna, Thomas
Sent: Thursday, December 17, 2015 2:43 PM
To: KevinDarryl.White@cslbehring.com; 'Angela.Azzara@cslbehring.com'
Subject: December 17, 2015 Information Request - BLA 125591.0 - Please Respond by January 8, 2016

CSL Behring Recombinant Facility AG
Attention: Mr. Kevin Darryl White
December 17, 2015
Sent by email

Dear Mr. White:

We are reviewing your May 29, 2015 biologics license application (BLA) for the following:

STN	Name of Biological Products
125591/0	Antihemophilic Factor (Recombinant), Single Chain

We determined that the following information is necessary to continue our review:

1. You provided method validation report (document #: MVR-24-314 rVIII-SC) for the (b) (4) endotoxin test qualification to be representative of (b) (4) the drug product by using of (b) (4) sample. Please provide a method validation for the actual (b) (4) actual drug product. A separate method validation is needed for each as the specifications for (b) (4) the drug product (b) (4) are different. The (b) (4) bacterial endotoxin test qualification reports should show that the (b) (4) drug product matrices are suitable for the intended test method (in accordance with (b) (4)). Please include maximal valid dilution, tested dilutions, positive product control percent recoveries, lot numbers with their respective potencies, final selected testing dilution and endotoxin test results. Furthermore, please include data for both the lowest (250 IU) and highest (3000 IU) potencies. If the testing dilutions are different per potency, please include a mid-range (1000 IU) potency as well.
2. You provided method validation report (document#:MVR-24-134) for the bioburden test qualification of your (b) (4) by using an (b) (4) sample, rather than the (b) (4) itself. Please provide a method validation report for the rVIII-SingleChain (b) (4) showing the (b) (4) is suitable for the intended test method in accordance with (b) (4). Please include data showing the recovery of (b) (4), initial microorganism counts, media/incubation information, relevant negative controls, and conformance lot numbers with their potencies.

3. You provided method validation report (MVR-25-022-rVIII) for the sterility test qualification of your drug product using a pilot scale lot representing the midrange (1000 IU [corresponding to a dosage of 400IU/ml]) potency. CBER requires that the sterility method validation be performed on the worst case scenario sample (i.e., the highest potency [3000 IU] {corresponding to a dosage of 600IU/ml}). Please qualify at least one lot of your drug product representing the highest potency showing the drug product matrix is suitable for the intended test method in accordance with (b) (4). Specifically, please include indicator microorganisms tested, their media, conformance lot numbers, and incubation conditions used in the qualification.

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 responses as an amendment to this file by January 8, 2016 referencing the date of this request.

The action due date for this file is May 28, 2016.

If you have any questions, please contact me.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP)^{CM}

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