From: Cagungun, Nannette
Sent: Tuesday, August 16, 2016 5:29 PM
To: Michele.Walsh@cslbehring.com
Subject: Information Request- C1 Esterase Inhibitor (Human)/CSL 830

Our Reference: BL 125606/0

Dear Ms. Walsh:

We are reviewing your June 30, 2016 biologics license application for C1 Esterase Inhibitor(Human). We are providing the following comments and request for information:

Bioburden

1. CBER finds the bioburden qualification report (Report No. MVR-24-134) unacceptable for the (b) (4) of C1-INH (b) (4) since the qualification was performed on the (b) (4) products. The method qualification should be performed on the proposed (b) (4) (Section 3.2.S.2.4.4-2). Therefore, please provide the bioburden qualification report for the C1-INH (b) (4) showing its (b) (4) is suitable for the intended test method in accordance with (b) (4) Please include data showing the (b) (4) microorganisms in the presence and absence of the (b) (4), (b) (4) for the samples tested.

2. According to the Q-24-134, the bioburden test method for (b) (4) samples was performed with (b) (4). However, CBER finds your bioburden method qualification incomplete and requests suitability be demonstrated in the presence of product performed with (b) (4), in accordance with (b) (4) In addition, please provide the (b) (4) results confirming the (b) (4) for all microorganisms tested.

Endotoxin

3. In your endotoxin qualification report (MVR-24-314 Berinert), the sample (b) (4) used in the method qualification was the CSLB's intravenous C1-INH product approved by FDA in 2009, which has a different (b) (4) C1-INH concentration. Therefore, CBER requests a qualification report showing the (b) (4) is suitable for testing using your (b) (4) Test method to include (b) (4), lot numbers of product tested, and selected product testing (b) (4).

Sterility

4. In section 3.2.P.5.1, please change the acceptance criterion from pass to (b) (4)

(b) (4)

5. You provided method validation report (MVR-25-002-Berinert) for the sterility test qualification of the Berinert®, as approved by FDA in 2009. Please provide the sterility test qualification report showing the test was qualified in accordance with (b) (4) to confirm the C1-INH concentrate product b) (4) is suitable for intended test method. Please include the following information to complete its review:

* (b) (4)

6. Please provide a detailed SOP used for Pyrogen testing, so CBER can ensure it was performed in accordance with b) (4)

Please submit your response to this information request as an amendment to this file by August 30, 2016 , referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If you have any questions, please do not hesitate to contact me.

Sincerely,

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