

From: Cagungan, Nannette
Sent: Friday, December 16, 2016 2:15 PM
To: Michele.Walsh@csllab.com
Subject: Information Request_CMC/Facility_C1INH/CSL830

Our Reference: BL 125606/0

Dear Ms. Walsh:

We are reviewing your June 30, 2016 biologics license application for C1 Esterase Inhibitor Subcutaneous (Human) for routine prophylaxis to prevent Hereditary Angioedema attacks in adult and adolescent patients. We are providing the following comments and request for additional information to continue our review:

1. Please reference 3.2.P.3.3-4, (b)(4) Filling and Packaging Procedure; page 9 of 9; Storage, you state that the product can be (b)(4) until lyophilization.

You also state the (b)(4) temperature in your recipe (b)(4)

a. Is this storage at (b)(4) part of the (b)(4) step? Please explain the disparity in the temperature ranges.

b. How did you establish the (b)(4) hold time?

2. Please provide a description (including manufacturer, item #, etc.) of the sterilizing filter used in (b)(4).

a. Please provide summary of the filter qualification (or re-qualification) performed associated with the more (b)(4).

3. Referencing your amendment, 125606/0.3 (received September 6, 2016): the Agency disagrees with your position statement.

The Agency concludes that your product is a co-packaged combination product, as defined by 21 CFR 3.2(e)(2). In this case, according to 21 CFR 4.4, you must demonstrate that the following provisions of the QS regulation have been satisfied:

- * Section 820.20: Management responsibility.
- * Section 820.30: Design controls.
- * Section 820.50: Purchasing controls.
- * Section 820.100: Corrective and preventive action

Please provide this information in a consolidated section of your BLA. The Agency suggests that you please reference Draft Guidance for Industry and FDA Staff: Current Good Manufacturing Practice Requirements for Combination Products (April 2015). (In particular, Section IV., What do I need to know about the CGMP requirements specified in 21 CFR 4.4(b)?)

4. For clarification, please identify when the following optimizations / improvements were made to the Mix2Vial presentation:

(b) (4)

A large rectangular area of the document is redacted with a solid grey fill. To the left of this redacted area, the text "(b) (4)" is visible, indicating a redaction under FOIA exemption (b)(4). The redaction covers several lines of text.

a. Please provide any validation or where appropriate verification, review, and approval of these design changes before their implementation.

Please submit the requested information in an amendment to the file by Friday, January 6, 2017, or as soon as possible 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 contact me at (240) 402-8267.

Sincerely,
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