

Information Request Email, May 10, 2013 - Novoeight

From: Pracht, Leigh
Sent: Friday, May 10, 2013 11:57 AM
To: 'LEWP (Lewis Pollack)'
Subject: RE: STN 125466 May 1, 2013 Information Request
Lewis,

Thanks for the information.

For the EMPQ of the Grade (b)(4) areas, it is acceptable to receive the response in June.

For the qualification of the DP formulation and filtration areas, Novo Nordisk can reference the November 30, 2012 CBE-30 (NovoSeven BLA #103665/5775); however you need to submit all the information in the amendment to the current BLA 125466. The information reported about the qualification of DP formulation and filtration areas, which was submitted to BLA 103665, needs to also be submitted to BLA 125466. This information should be provided in June 2013 to have enough time to review it within this BLA cycle.

Best regards,
Leigh A. Pracht
Regulatory Project Manager
FDA/CBER/OBRR/DBA
WOC1; RM562N; HFM-380
1401 Rockville Pike
Rockville, MD 20852
Telephone: 301-827-6116
Fax: 301- 827-2857
Leigh.Pracht@fda.hhs.gov

From: LEWP (Lewis Pollack) [mailto:lewp@novonordisk.com]
Sent: Friday, May 10, 2013 11:21 AM
To: Pracht, Leigh
Subject: RE: STN 125466 May 1, 2013 Information Request

Dear Leigh,

Novo Nordisk is planning to submit the responses for the (b)(4) facility on May 17, 2013, as requested. However, additional time will be required to provide the EMPQ for the Novo Nordisk drug substance (DS) facility. We also would like to describe our response plan for the request on Novo Nordisk's drug product (DP) facility. These items are highlighted below in your May 1, 2013 email.

DS Facility EMPQ

Novo Nordisk is not able to provide the EMPQ for the Grade (b)(4) areas in the (b)(4) facility by May 17. Due to the -----(b)(4)-----, the EMPQ is still on-going. We plan to submit two EMPQ reports for the Grade (b)(4) areas on June 14, 2013 as discussed with the investigator at the PLI and committed to in the May 1 responses to the 483 observations.

DP Facility Qualification

The qualification data for the changes to the DP formulation and filtration areas were submitted as a CBE-30 to the NovoSeven BLA #103665/5775 on November 30, 2012 (Sequence #148). The action date is June 1, 2013. The facility changes also were discussed with FDA on May 2, 2012. The meeting minutes (attached) state on page 6 that "Future product introduction in the Fill Line (b)(4) manufacturing area can be introduced as a CBE-30 with one conformance lot." To avoid submission and review of redundant information, Novo Nordisk proposes to reference the November 30, 2012 CBE-30 and include only information that would have gone into a CBE-30 for a future product introduction. We will, however, provide information on both conformance lots.

Please contact me with FDA's concurrence with our plans or if there are any concerns.

Regards,
Lewis

From: Pracht, Leigh [mailto:Leigh.Pracht@fda.hhs.gov]
Sent: Wednesday, May 01, 2013 11:54 AM
To: LEWP (Lewis Pollack)
Subject: STN 125466 Information Request
Our Reference: BL 125466/0
Novo Nordisk Inc.
Attention: Lewis Pollack, PhD
May 1, 2013
Sent by email

Dear Dr. Pollack:

We are reviewing your October 15, 2012 biologics license application (BLA) for Antihemophilic Factor (Recombinant), Plasma/Albumin Free [NovoEight]. We determined that the following information is necessary to continue our review:

The following comments are to get clarification and additional information about the manufacturing of the 0.9% NaCl diluent at -----(b)(4)----- facility in (b)(4).

1. You stated that visual inspection of the final product is performed per (b)(4) SOPs. Please describe the visual inspection procedure, what defects are being evaluated, what are the acceptance criteria, and the criteria for accepting or rejecting a lot. Please clarify if the inspection is manual, semi automated or automated.
2. You stated that container closure integrity --(b)(4)--- test was performed on 0.9% NaCl PFS containing -(b)(4)- that had been subjected to -----(b)(4)--- ----- cycles to cover a worst case scenario, and that no -----(b)(4)----- was detected by visual inspection. Please provide the studies performed to demonstrate the validation of this method – conditions under which ---(b)(4)----- was performed as well as positive and negative controls.

3. Please clarify if any part of the container closure system that is product contact contains latex. Aside from the depyrogenation of the syringe, do you evaluate and mitigate the endotoxin level of other product contact parts of the container closure? Please explain.

4. Please clarify if the filling equipment (or which part) is dedicated for the manufacture of 0.9% NaCl diluent. Please provide a summary of the validation studies performed to demonstrate cleaning and sterilization of the filling equipment.

5. You provided a summary report of the sterilization of the final product. Please describe the (b)(4) and the sterilization method. You stated that the -----(b)(4)----- of the -----(b)(4)---- showed no -----(b)(4)----, please provide a schematic diagram showing the -----(b)(4)----- and the justification why they represent coverage of the -----(b)(4)---- (and worst case ---(b)(4)--). Please also provide the -----(b)(4)----- and -----(b)(4)-----, and why these ---(b)(4)---- are considered representative (or worst case) --(b)(4)--.

6. Please list the number of --(b)(4)-- that support the production of 0.9% NaCl diluent and their uses.

7. You stated that equipment and primary packaging materials are sterilized using ---(b)(4)----. Please describe the -(b)(4)- and the sterilization method. Please provide the sterilization validation studies, including the different (b)(4) qualified.

8. In section 3.2.A.1 Facilities and Equipment Report for Sodium Chloride manufacturing facility, you stated that Sodium Chloride is currently classified as a -----(b)(4)----- for cleaning. Please provide results of studies performed to demonstrate that NaCl is the -----(b)(4)-----, and provide summary reports of studies performed to validate the cleaning procedures.

9. You stated that CIP/SIP is used for cleaning and sterilization of equipment. Please describe the parameters used, and provide the results of studies performed to validate the CIP/SIP process. Please list the equipment cleaned/sterilized by CIP/SIP.

10. In the submission, there is a brief description of the facility water. As (b)(4) is used as an ingredient in the manufacture of the diluent, please describe your procedures for monitoring the quality of the (b)(4).

11. Please describe your procedures for packaging and shipping the 0.9% NaCl to Novo Nordisk facilities.

The following letter ready comments pertain to the manufacturing of Turoctocog alfa drug substance and drug product at Novo Nordisk facilities in Denmark.

1. Please submit the container closure testing performed to demonstrate the integrity of the container closure of the final drug product.

2. During the PLI, you stated that you implemented changes to the areas used for formulation and filtration of the drug product; and that two Batches of Turoctocog alfa for clinical trials were manufactured in week 10, 2013 (after implementing the changes) . Please submit the qualification of the area as an amendment to BLA 125466/0.

3. Please provide the EMPQ for the Grade (b)(4) areas in the -(b)(4)-- facility, and include the frequency and acceptance criteria (alert and action limits) for routine monitoring.

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 response to this information request as an amendment to this file by May 17, 2013 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.

The action due date for this file is October 15, 2013.

If you have any questions, please contact me at (301) 827-6116.

Sincerely,

Leigh A. Pracht

Regulatory Project Manager

FDA/CBER/OBRR/DBA

WOC1; RM562N; HFM-380

1401 Rockville Pike

Rockville, MD 20852

Telephone: 301-827-6116

Fax: 301- 827-2857

Leigh.Pracht@fda.hhs.gov

THIS MESSAGE IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify the sender by e-mail or phone.

Page Last Updated: 11/15/2013

Note: If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

Language Assistance Available: [Español](#) | [繁體中文](#) | [Tiếng Việt](#) | [한국어](#) | [Tagalog](#) | [Русский](#) | [ةيبرعلا](#) | [Kreyòl Ayisyen](#) | [Français](#) | [Polski](#) | [Português](#) | [Italiano](#) | [Deutsch](#) | [日本語](#) | [ىسراف](#) | [English](#)