

From: Maruna, Thomas
Sent: Wednesday, June 08, 2016 2:53 PM
To: 'Janice Castillo'
Cc: Ovanesov, Mikhail V.; Harman, Christine
Subject: 08-Jun-2016 Information Request ((b) (4)-Facility) - BLA 125586.0 - Response Required by Dates Below

Importance: High

Portola Pharmaceuticals Inc.
Attention: Ms. Janice Castillo
June 8, 2016
Sent by email

Dear Ms. Castillo:

We are reviewing your December 17, 2015 biologics license application (BLA) for the following:

STN	Name of Biological Products
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125586/0	Coagulation Factor Xa (Recombinant), Inactivated
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1. Please indicate a timeframe for when responses to an, outstanding information request from DMPQ (specifically, (b) (4) facility, items 19-28) sent on April 6, 2016, will be provided. Please note that this information is necessary for the BLA review.
2. In regards to the information provided in Amendment 33 (received May 27, 2016), including the lyophilization cycle charts and monitoring information of the (b) (4) [REDACTED], and lyophilization mapping samples, please note and respond to the following:
 - a. The lyophilization cycle charts provided did not provide sufficient details as to determine what is being assessed and monitored. Please describing the information provided in the graph (i.e indicate scales, and labels for (b) (4) [REDACTED], in addition to labeling of the stage of the cycle ((b) (4) [REDACTED])).
 - b. Please indicate where the data listed in the “Lyophilization Cycle Monitoring forms” for Lot (b) (4) [REDACTED] and Lot (b) (4) [REDACTED] originates from (i.e. are these values handwritten from an electronic readout or are these values pulled from the chart recordings that were provided). Additionally, please indicate the timepoints used for monitoring critical lyophilization parameters, for example are the critical parameters monitored every 10 min, every hour etc. and provide a justification for why the time interval for monitoring the parameters was used. It should be noted that in the Lyophilization Cycle Monitoring form, there is no column for product

temperature values. Please indicate if product temperature was monitored during the validation runs.

- c. Please clarify how QA determines that the critical process parameters for (b) (4) and time were met for (b) (4).
- d. In regards to the lyophilization mapping samples, you indicated that (b) (4) samples for Lot (b) (4) and (b) (4) samples for Lot (b) (4) were tested from each (b) (4) of the freeze dryer. Please provide the product testing results for these additional samples as Tables 3.2.P.3.5-13 and 3.2.P.3.5-14 only provide one testing results for each sampled (b) (4).

The review of this submission is on-going and issues may be added, expanded upon, or modified as we continue to review this submission.

You are required to submit your responses as an amendment to this file by the following dates:
Question #2 (a-d) - no later than **June 24, 2016** / Question #1 – **ASAP**.

The action due date for these files is August 17, 2016.

If you have any questions, please contact me.

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH
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