

From: Maruna, Thomas  
Sent: Wednesday, May 04, 2016 2:27 PM  
To: 'Janice Castillo'  
Cc: Bhattacharyya, Lokesh; Ovanesov, Mikhail V.; Lee, Timothy;  
Valencia,  
Iliana  
Subject: RE: Sample Request - BLA 125586.0 - Respond by May 10. 2016

Importance: High

Janice,

Thank you for sending us a 10 mL sample of lyophilized material. However, this is not the material we requested in our Information Request, dated May 3, 2016. Your response is not consistent with our request.

Please provide 10 mL of formulated Coagulation Factor Xa (Recombinant), Inactivated drug product (STN: 125586) obtained from the manufacturing line before the lyophilization step for evaluation in our laboratory in support of your BLA submission. You may send us non-cGMP drug product (but not drug substance) in lieu of the drug product formulated under cGMP, as long as the product is scientifically representative of the drug product final formulation. We request that you send us the sample within 2 weeks (i.e. by May 18, 2016) of receiving this request. If you are unable to do so, please let us know the date when you will be able to send us the requested materials. If you are unable to send us the requested material within 2 weeks, please let us know when you will be able to do so.

Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH  
Lieutenant, U.S. Public Health Service  
Senior Regulatory Management Officer  
FDA/CBER/OBRR/IO  
thomas.maruna@fda.hhs.gov  
Office: (240) 402-8454

From: Janice Castillo [mailto:jcastillo@Portola.com]  
Sent: Wednesday, May 04, 2016 11:36 AM  
To: Maruna, Thomas  
Cc: Campbell, Karen M; Ovanesov, Mikhail V.  
Subject: RE: Sample Request - BLA 125586.0 - Respond by May 10. 2016

Thomas,

We sent a 10 mL sample of lyophilized material on 20 April along with instructions for reconstitution, and you have asked for formulated material prior to lyophilization. Our rationale for sending the lyophilized material follows.

Product sent to (b)(4) for fill/finish is formulated drug substance. (b)(4) uses this formulated drug substance as is for fill finish. Hence, there is no difference between this material and reconstituted lyophilized drug product. Additionally, (b)(4) is currently in shutdown for routine maintenance, and Portola does not have any formulated drug substance at (b)(4) awaiting fill/finish. Please ask the lab how they would like us to proceed. I am happy to have a phone call regarding this matter if it would help.

Regards,  
Janice

Janice Castillo  
Senior Vice President, Regulatory Affairs and Quality Assurance  
Portola Pharmaceuticals, Inc.  
South San Francisco, CA 94080  
Direct Tel: 650-246-7360  
Cell phone: 650-867-6984  
email: jcastillo@portola.com

From: Maruna, Thomas [mailto:Thomas.Maruna@fda.hhs.gov]  
Sent: Tuesday, May 03, 2016 10:41 AM  
To: Janice Castillo  
Cc: Campbell, Karen M; Ovanesov, Mikhail V.  
Subject: Sample Request - BLA 125586.0 - Respond by May 10. 2016

Janice,

Please provide 10 ml of formulated Coagulation Factor Xa (Recombinant), Inactivated drug product (STN: 125586) obtained from the manufacturing line before the lyophilization step for evaluation in our laboratory in support of your BLA submission. You may send us non-cGMP drug product (but not drug substance) in lieu of the drug product formulated under cGMP, as long as the product is scientifically representative of the drug product final formulation. We

request that you send us the sample within 2 weeks of receiving this request. If you are unable to do so, please let us know the date when you will be able to send us the requested materials.

Please ship the sample to the address listed below:

Mark Levi  
Center for Biological Evaluation and Research  
Division of Biological Standards and Quality Control  
10903 New Hampshire Avenue  
W075, G-662  
Silver Spring, MD 20993-0002

Very Respectfully,

Thomas J. Maruna, MSc, MLS(ASCP), CPH  
Lieutenant, U.S. Public Health Service  
Senior Regulatory Management Officer  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
Office of Blood Research and Review  
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