

RECORD OF TELEPHONE CONVERSATION

Submission Information

Application Type	BLA
STN	125586/0
Review Office	OBRR
Applicant	Portola Pharamceuticals / Lic. # 2017
Product	Coagulation Factor Xa (Recombinant), Inactivated
Trans-BLA Group:	No

Telecon Details

Telecon Date/Time	05-MAY-2016 12:30 PM ET
Author	MARUNA, THOMAS J.
Outside Phone Number	1-877-668-4490
FDA Originated?	NO
Communication Categories	IR – INFORMATION REQUEST
Related STNs	None
Related PMCs	None
Telecon Summary	Discussion with Portola: May 3, 2016, Information Request for Sample Submission
FDA Participants	Bhattacharyya, Lokesh; Lee, Timothy; Levi, Mark; Maruna, Thomas; Ovanesov, Mikhail; Verdun, Nicole
Applicant Participants	Andrew Ramelmeier, PhD, Senior Vice President Technical Operations, Biologics Janice Castillo, Senior Vice President Regulatory Affairs and Quality Assurance Aditya Wakankar, PhD, Associate Director, Pharmaceutical Development

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Telecon Body:

Background

FDA sent the following Information Request (IR) to Portola on May 3, 2016:

*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
WO75, G-662
Silver Spring, MD 20993-0002*

In an email response received on May 4, 2016, Portola stated that they provided samples on April 20, 2016; FDA noted that these samples did not satisfy the original request because the material was lyophilized Drug Product (DP). Portola was informed of the error and the request was repeated. Consequently, Portola requested a teleconference to discuss and clarify the IR dated May 4, 2016.

Discussion

FDA reiterated its request that we need Drug Product (DP) intermediate material that was formulated but not lyophilized to allow investigation to address the following:

1. Adequacy of the sponsor's method to detect and quantitate (relative) aggregates and sub-visible particles in the drug product.
2. If the (relative) amount of aggregates and sub-visible particles in the drug product obtained in the DBSQC lab are consistent with those reported by the sponsor?
3. Is there a significant increase in the amount of aggregates and sub-visible particles due to lyophilization of the drug product formulation, including the effect of the drug product matrix.

Therefore, evaluation of DS alone will be inadequate to evaluate the difference between liquid DP intermediate and DP following lyophilization. FDA further reiterated that the material provided need not be cGMP compliant provided that Portola could assure the samples were scientifically representative of the DP final formulation.

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Portola maintained that there is no difference between the samples provided on April 20, 2016, and reconstituted lyophilized drug product requested. Further, Portola noted that DP manufacturer (b) (4) is currently in shutdown for routine maintenance and the DP intermediate material would not be available until the end of May or early June 2016. Portola suggested that a representative sample of DS formulated adequately to represent the drug product intermediate before the lyophilization step could be obtained from (b) (4) and could be provided as early as Tuesday, May 10, 2016. Portola would also provide the requested samples from (b) (4) once they were back online (i.e. late May/early June). Portola stated that the samples would arrive frozen. FDA agreed to Portola's proposal and requested a description of the material be submitted to the Regulatory Manager in advance of sample submission. Portola agreed to provide the requested description.

END