

From: Maruna, Thomas
Sent: Wednesday, February 17, 2016 1:31 PM
To: 'Janice Castillo'
Cc: Bhattacharyya, Lokesh
Subject: Request for Standards, Reagents and Samples for BLA 125586.0 - Please Submit by March 2. 2016

Importance: High

Attention: Ms. Janice Castillo
February 17, 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
125586/0	Coagulation Factor Xa (Recombinant), Inactivated

We request that you provide us the following standards, reagents and samples for the implementation of the test methods in the CBER laboratory and/or testing in-support of your BLA submission (STN: 125586) by March 2, 2016. If you are unable to do so by the requested date, please let us know the date when you will be able to send us the requested materials.

1. Direct Potency Assay

Please provide sufficient quantities of each of the following to carry out 25 assays.

- a. Reference Standard
- b. Assay Control
- c. (b) (4) Inhibitor
- d. FXa, for preparing Diluted FXa (as per your Table 3.2.S.4.2.-2)
- e. Drug product: We need samples of the drug product for evaluation and implementation of the test method in our laboratory and to subsequently perform in-support testing. For evaluation and implementation of the test method in our laboratory, we may use 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 for the assay. In addition, we require one vial each from (b) (4) lots of your drug product manufactured under full cGMP for in-support testing. If you do not have (b) (4) lots available, please notify CBER for additional information.

2. Indirect Potency Assay

Please provide sufficient quantities of each of the following to carry out (b) (4) assays.

- a. Reference Standard
- b. Assay Control
- c. FXa Inhibitor (b) (4),
- d. (b) (4)
- e. FXa, for preparing Diluted FXa, 0.125 µg/mL (as per your Table 3.2.S.4.2-3)
- f. Drug product: We need samples of the drug product for evaluation and implementation of the test method in our laboratory and to subsequently perform in-support testing. For evaluation and implementation of the test method in our laboratory, we may use 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 for the assay. In addition, we require one vial each from (b) (4) lots of your drug product manufactured under full cGMP for in-support testing. If you do not have (b) (4) lots available, please notify CBER for additional information.

3. In addition, please provide,
 - a. The test results for each of the drug product lot,
 - b. The assigned values for the reference standards requested,
 - c. The assigned values and acceptance limits/ranges for assay controls requested,
 - d. COA, if available, or concentrations and other information necessary to perform the assay for the reagents requested (e.g., (b) (4) and FXa).

Ship reagents, standards, controls and drug product samples to the address listed below:

Grainne Tobin
Center for Biological Evaluation and Research
Division of Biological Standards and Quality Control
10903 New Hampshire Avenue
WO75, G-717
Silver Spring, MD 20993-0002

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

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
Lieutenant, U.S. Public Health Service
Senior Regulatory Management Officer
Food and Drug Administration
Center for Biologics Evaluation and Research

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