



Our STN: BL 125506/0

Bio Products Laboratory

Attention: (b) (4)

Dear (b) (4) :

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated July 10, 2013 for Coagulation Factor X (Human) to determine its acceptability for filing. Under 21 CFR 601.2(a), we have filed your application today. The review classification for this application is Priority. Therefore, the review goal date is March 11, 2014. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which include the timeframes for FDA internal milestone meetings. We plan to hold our internal mid-cycle review meeting on November 6, 2013. Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process.

We will contact you regarding your proposed labeling no later than February 9, 2014. If post marketing study commitments (506B) are required, we will contact you no later than February 9, 2014.

At this time, we have no plans to present this application to an Advisory Committee.

While conducting our filing review, we identified the following potential review issues:

Please provide the following completed validation studies, including protocols and report summaries (data) for our review:

1. Lyophilizers^{(b) (4)}: studies and results to support the lyophilization of Factor X in the lyophilizers including sampling plan (samples collected from every shelf) and results of testing performed to demonstrate consistent lyophilization of Factor X throughout all the shelves of every lyophilizer.
2. Environmental Monitoring Performance Qualification of the formulation/filling/lyophilization and capping areas under static and dynamic conditions.
3. Cleaning of product contact equipment for Factor X and WFI diluent: (b) (4).
4. Cleaning and sterilization of the lyophilizers.
5. (b) (4) Autoclave (b) (4) validation studies to support its use for terminal sterilization of WFI diluent.
6. Vial washer and depyrogenation tunnel: studies performed, acceptance criteria, and results to demonstrate the validation of the cleaning and depyrogenation for Factor X 10-mL molded tubes, and WFI 5-mL tube drawn vials.
7. Visual Inspection: Qualification of the 100% visual inspection; description of the critical, major and minor defects, and the acceptance criteria for the batch to be considered as passing visual inspection, and the conditions under which a second and third visual inspection is allowed.
8. AQL testing and the acceptance criteria for a batch to be considered as passing.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Pratibha Rana, at (301) 827-6124.

Sincerely yours,

Iliana Valencia, MS
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