

Mid-cycle Communication Teleconference

Application type and number: BLA STN 125506/0
Product name: Coagulation Factor X (Human)
Proposed Indication: Treatment of patients with hereditary Factor X deficiency
Applicant: Bio Products Laboratory (BPL)
Meeting date & time: November 21, 2013, 10:30 am - 12:00 pm
Committee Chair: Mikhail V. Ovanesov, PhD
RPM: Pratibha Rana, MS

BPL Attendees:

David Wilson, Technical Director
Peter Feldman, Coagulation Factor Team, Manager
Matt Bodiam, Technical Development Manager
Joanne Lloyd, Project Scientist, R&D
Miranda Norton, Clinical Project Leader
Kate Gillanders, Clinical Research Manager
Terry Gree, Validation Manager
Azhar Salahudeen, Senior Qualified Person
Peter Roberts, Senior Validation Engineer
Mauricio Gil, Regulatory Affairs Project Manager

(b) (4)

FDA Attendees:

Pratibha Rana, MS, Regulatory Project Manager, CBER/OBRR/DH/LH
Mikhail V. Ovanesov, PhD, CMC Reviewer, CBER/OBRR/DH/LH

Eastern Research Group (ERG) Attendee:

Christopher Sese, Independent Assessor, ERG

DISCUSSION SUMMARY:

1. The review committee identified the following two significant issues:
 - a. Method validation is deficient for 13 analytical methods, and
 - b. Process validation is deficient in several processes, for example: (i) lyophilization; (ii) cleaning and sterilization of lyophilizers; and (iii) Grade (b) (4) monitoring under dynamic conditions. Multiple failures (6 out of (b) (4) batches) in manufacture could be attributable to deficiencies in process validation.
2. Outstanding issues that BPL has not fully addressed:

- a. FDA had summarized the deficiencies in analytical method validation in an information request to BPL dated 9 October 2013. BPL, in response, proposed to complete method validation by 31 January 2014. However, BPL has not indicated when it will submit the validation reports to the FDA.
- b. Deficiencies in process validation were cited as objectionable observations in Form FDA 483 at the conclusion of the pre-license inspection on 25 October 2013. BPL proposed to complete process validation by 30 June 2014, but did not indicate when it will submit the completed reports to the FDA.

FDA would like to point out that the action due date of this BLA is 11 March 2014, and the inability to adequately address the information requests and inspectional observations by the action due date will result in the reiteration of the outstanding deficiencies in the Complete Response letter.

3. The review committee did not identify major safety concerns to date.
4. Currently, the review committee does not think that a Risk Evaluation and Mitigation Strategy is required.
5. The review committee has identified new information requests that will be communicated to BPL. FDA will request (1) clarification on recovered plasma used; (2) clarification on plasma stability studies; (3) specifications for the (b) (4) Factor X bulk; (4) correct lot release protocol; (5) final clinical study report; (6) inclusion of pediatric and pregnant patients in the Pharmacovigilance Plan and collection of adverse event data when off-label use is identified; and (7) additional Factor X samples and reagents for the NaPTT assay.
6. The late-cycle meeting is currently scheduled for January 16, 2014, 11:30 am - 1:00 pm.
7. This BLA will not be presented at the Blood Products Advisory Committee.

END