

MEMORANDUM



Department of Health and Human Services
Public Health Service
United States Food and Drug Administration
Center for Biologics Evaluation and Research



From: Mikhail V Ovanesov, PhD, Committee Chair and Product Reviewer
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Research and Review (DHRR)/OBRR

To: Basil Golding, MD, Director, DHRR/OBRR

Subject: Designation of STN 125582/0.34 as a Major Amendment

DESIGNATION OF AMENDMENT 125582/0.34 AS MAJOR

Biologics License Application (BLA), STN 125582/0, for Coagulation Factor IX (Recombinant), Albumin Fusion Protein, with the proprietary name IDELVION was submitted by CSL Behring Recombinant Facility AG (CSLB) on 5 December 2014. The application is on a standard review schedule under the PDUFA V Program, with the action due date on 5 December 2015.

On 31 August 2015, CSLB submitted amendment STN 125582/0.34 containing responses to CMC questions regarding deficient method validations, which were conveyed to the company in an information request dated 12 June 2015 and during the Pre-Approval Inspection (PAI). On behalf of the review committee for the BLA under STN 125582/0, and based on the review of the amendment and SOPP 8402, I recommend the designation of STN 125582/0.34 as a Major Amendment.

JUSTIFICATION FOR MAJOR AMENDMENT DESIGNATION

SOPP 8402 and the PDUFA V Program define a Major Amendment as a submission of information to a pending application that extends the review clock. According to section V.D. of SOPP 8402, an amendment may be qualified as major when it contains a substantial amount of new manufacturing information and data not previously submitted to or reviewed by the Agency.

Amendment STN 125582/0.34 contains substantive revisions to sections 3.2.S.2.4 Controls of Critical Steps and Intermediates, 3.2.S.4.3 Validation of Analytical Procedures and 3.2.P.5.3 Validation of Analytical Procedures. The applicant provided new validation reports for the 6 key analytical procedures, related to process development, process validation and manufacturing controls.

The changes proposed in amendment STN 125582/0.34 are part of a larger series of CMC amendments that are meant to address the deficiencies in method validation (Amendments 19, 20, 25, 27, 30, 34, and 36 received on 23 June, 30 June, 29 July, 31 July, 10 August,

31 August, and 4 September, respectively), justifications of specifications (Amendments 19, 23, 30, 32, and 37 received on 23 June, 15 July, 10 August, 14 August, and 4 September 2015, respectively), and comparability studies (Amendments 17, 29, 40 and 41 received on 12 June, 7 August, 18 September 2015, and 18 September 2015, respectively) that could be traced back to deficiencies identified during the facility inspection.

Since amendment STN 125582/0.34 contains a substantial amount of new information and analysis (more than 300 pages), STN 125582/0.34 may be classified as a Major Amendment. In addition, this submission is also linked to future amendment(s) projected to be submitted to us close to the action due date of 5 December 2015. For example, on 18 September 2015, CSLB submitted amendments 40 and 41, containing documents that are close to 400 pages total on new information regarding analytical comparability. Taken together, it is highly justified that the review schedule of this BLA be extended to allow thorough reviews of the new information.

NEW ACTION DUE DATE

According to section V.E.1.b of SOPP 8402 and the PDUFA V Program, a Major Amendment extends the action due date of an original application by three months. If the Major Amendment designation receives concurrence by the Director, Division of Hematology Research and Review, OBRR, the new action due date for BLA STN 125582/0 will be **4 March 2016**.