



MEMORANDUM

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

To: Timothy Lee, Acting Chief, LH /DHRR/OBRR, Mikhail Ovanesov, Chair, LH /DHRR/OBRR, File of BLA STN 125582/0 & Edward Thomson, RPM

From: Chava Kimchi-Sarfaty, CMC reviewer, Laboratory of Hemostasis, DHRR/OBRR

Subject: Review of CMC information regarding (b) (4) in BLA STN 125582/0 for albumin-factor IX fusion protein (rIX-FP) by CSL Behring indicated to treat patients with hemophilia B for: (1) Routine prophylaxis to prevent or reduce the frequency of bleeding episodes, (2) Control and prevention of bleeding episodes and (3) Control and prevention of bleeding in the perioperative setting

I. Background

This memorandum summarizes the review of the CMC information in CSL Behring’s BLA 125582/0 to evaluate the safety and efficacy of recombinant factor IX albumin fusion protein (rIX-FP) specifically regarding the (b) (4) technique that was used to construct the recombinant factor IX (rFIX).

rIX-FP is a recombinant protein for which the nucleotide sequence was (b) (4). Furthermore, to increase protein stability the rFIX is fused through a cleavable linker to albumin. This approach seems to increase the stability of the protein.

Broadly, (b) (4)

II. Scope of the review

Research experience with (b) (4) FIX

In the past several years, we have examined in the laboratory (b) (4) different FIX (b) (4) and all revealed changes in the three-dimensional structure of the protein and/or its post-translational modifications. These are all mostly slight changes, but we do not know how they affect the protein characteristics including immunogenicity.

(b) (4) study of rFIX by CSL

3 Pages determined to be not releasable: (b)(4)