



MEMORANDUM

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

To: File of STN 125582/0 & Edward Thomson, RPM

From: Chava Kimchi-Sarfaty, Zuben Sauna, CMC consultants, Laboratory of Hemostasis, DHRR/OBRR

Subject: Final review of CMC information regarding functional characterization in BLA for albumin-factor IX fusion protein (rIX-FP) by CSL Behring

Through: Mark Weinstein, Associate Deputy Director, OBRR
Basil Golding, Director, DHRR/OBRR

I. Background

This memorandum summarizes the review of the CMC information in CSL Behring's (CSL) BLA under STN 125582/0 to evaluate the safety and efficacy of recombinant factor IX albumin fusion protein (rIX-FP), specifically regarding the functional characterizations that were used to compare rIX-FP with a licensed recombinant factor IX (rFIX) product, (b) (4).

Module 3 – Quality, submitted on 12.17.2015, did not contain all the information regarding the assays used to characterize rIX-FP. An information request was sent to CSL on February 2, 2016 and their response was received on February 8, 2016.

FDA IR #1:

In Module 3 – Quality (submitted on 12.17.2015), Table 3.2.S.3.1.2-2, you presented the (b) (4) activity of rIX-FP from a commercial scale vs. (b) (4). The rIX-FP showed a (b) (4) activity of (b) (4), while the (b) (4) activity for the recombinant Factor IX (b) (4) was (b) (4).

1. Please provide information about the assay standard and reagents that were used to calculate the (b) (4) activity for this Table.

CSLB Response to FDA Request #1:

The assay standard used for calculation of the (b) (4) activity of rIX-FP in Table 3.2.S.3.1.2-2 was the WHO (b) (4) International Standard for Factor IX concentrate.

The (b) (4) used in the Factor IX coagulation assay was (b) (4).

The (b) (4) activity of recombinant Factor IX stated in Table 3.2.S.3.1.2-2 is based on published material (b) (4). The (b) (4) potency determined for labeling refers to potency determined against the WHO International Standard for Factor IX concentrate; therefore CSL assumed that the (b) (4) activity from the literature citation is based on the WHO International Standard.

Reviewers' comment:

The response is satisfactory.

FDA IR #2:

Please provide the lot number for the rFIX-FP that was used to make this comparison.

CSLB Response to FDA Request #2:

CSLB provided the information requested; the lot number for the rIX-FP used for the comparison in Table 3.2.S.3.1.2-2 is (b) (4)

Reviewers' comment:

The response is satisfactory.

FDA IR #3:

Please provide (b) (4) activities for all three commercial lots, the average, and the SD results.

CSLB Response to FDA Request #3:

CSLB provided the information requested:

(b) (4)

Reviewers' comment:

The response is satisfactory.

FDA IR #4:

For the (b) (4) activity measurements you used similar protein concentrations of rFIX-FP and (b) (4) in the test (determined by (b) (4), and confirmed by (b) (4)). However, it is unclear whether the same concentrations of these proteins were used in the other tests reported in this Module. Please clarify if, in fact, this is the case for these other tests.

CSLB Response to FDA Request #4:

The comparison basis appears in Table 2 below:

Table 2: Comparison Basis for rIX-FP and (b) (4) used in the Functional Characterization of IDELVION

(b) (4)

(b) (4)

Reviewers' comment:

The response is satisfactory. The (b) (4) activity of rFIX-FP is (b) (4) than that of (b) (4) taking in consideration the (b) (4). All other assays that evaluate the intermediate steps, namely, (b) (4) (b) (4) show equivalent activities for rFIX-FP and (b) (4). The source of the (b) (4) difference in (b) (4) activities of rFIX-FP and (b) (4) was discussed earlier with CSL and the CMC review team found CSL explanation satisfactorily.

II. Conclusions

CSL responded adequately to these IRs.