



MEMORANDUM

To: Review Committee Chair

From: Parmesh Dutt, PhD, Biologist, LBRP, DBSQC, OCBQ

Through: Kori Francis, Branch Chief, LBRP, DBSQC, OCBQ
Maryna Eichelberger, PhD, Director, DBSQC, OCBQ

Sponsor / Product:

Octapharma /BALFAXAR(Octaplex). Human plasma derived prothrombin complex concentrate containing Coagulation Factors II, VII, IX, X, Protein C and Protein S, STN: 125776

Subject: In-support testing to measure factor IX activity using Factor IX (b) (4) (b) (4) assay for Licensing Action of BALFAXAR, STN 125776.

Background: A request was made by the review committee Chair to measure the Factor IX activity in three lots of BALFAXAR, using the (b) (4) assay for factor IX.

Method: The factor IX potency of three lots of BALFAXAR was measured at LBRP/DBSQC/OCBQ/CBER using a factor IX (b) (4) assay with a Diagnostica Stago STA Compact Max Analyzer. The method detailed in Document ID # 000374 was used to measure factor IX potency with some minor changes. The following reagents were used as per the sponsor's test method.

- Activating Reagent – (b) (4) was replaced with (b) (4)
- (b) (4) Reference Standard (b) (4) Human Coagulation factor IX concentrate (b) (4) batch (b) (4) This material has also been established as (b) (4) (b) (4) for blood Coagulation Factor IX, concentrated. It has a labelled potency of (b) (4) (supplied by sponsor). We also used (b) (4) (b) (4) for a comparison.
- Corporate positive control, drug product Lot # (b) (4) 1000 IU, reconstituted volume 40 mL (29.1 IU/mL- nominal value as per COA, provided by sponsor).
- For the initial dilutions of Standard, Control and Samples, in place of the FIX deficient plasma, (b) (4) was supplemented with (b) (4) Measurements were made at three dilutions of each sample within the testing range of the validated method; the results reported (Table 1) are the mean of the three IU/mL values.

- (b) (4) (b) (4) (b) (4) (b) (4) of product at (b) (4) FIX dilution. Thereafter the dilutions to (b) (4) (b) (4) were made with (b) (4) for storage of (b) (4) product aliquots at (b) (4) (b) (4). On the day of testing the products were diluted in (b) (4) to (b) (4) (b) (4) FIX potency before final three testing dilutions, again in (b) (4)

Results:

- The standard curve was derived by the linear regression analysis from the clotting times obtained using both the (b) (4) (currently in use (b) (4) at DBSQC) or the (b) (4) Standard provided by sponsor. The standard curves met the validity criteria (R^2 (b) (4)) for the tests with (b) (4) using the (b) (4) Standard or the (b) (4) standard respectively (Table1).
- The factor IX potency of the corporate control (b) (4) measured (b) (4) with (b) (4) using (b) (4) or the (b) (4) Standard respectively. The results are within the DBSQC test method acceptable range (80-120%) for the control sample at (b) (4) of the sponsor's COA Value of 29.1 IU/mL (Table 1).
- The % RSD for measurement of three dilution sets for all three lots are in between 2.8 -9.9 % and therefore meet the CBER/DBSQC assay validity criteria of $\leq 10\%$.

The potency assay results are summarized in Table 2 below, which also shows the sponsor's results and proposed specifications.

Conclusions:

Factor IX potencies for all the three lots submitted by sponsor for evaluation by DBSQC/CBER are within the proposed specification limits. The potency results obtained at the DBSQC/CBER laboratory are consistent with those obtained by the manufacturer. The results for control and all three samples tested at the DBSQC/CBER meet the assay validity criteria and specifications proposed by the sponsor.

Table 1: Standard Curve and Control acceptance criteria



Table 2: FDA / CBER FIX potency measurement using the factor IX (b) (4) assay

Lot Number	Manufacturer		CBER/OCBQ/DBSQC		CBER/ Manufact urer Ratio (%)
	Proposed BLA Specification (IU/mL)	Factor IX Potency Assay Results (IU/mL) *	Factor IX Results Mean from 3 Dilutions (IU/mL)	% CV	
(b) (4) (500 IU/vial)	20- (b) (4)	24	24.67	9.9	102.79
(b) (4) (500 IU/vial)	20- (b) (4)	22	22.62	2.8	102.81
(b) (4) (1000 IU/vial)	20- (b) (4)	29	27.02	6.8	93.17

* Data in Certificate of Analysis, provided by the sponsor