Laboratory Validation of CRYO*check*™ Chromogenic Factor VIII Across Multiple Coagulation Analyzers

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Introduction

CRYO*check* Chromogenic Factor VIII (Precision BioLogic, Dartmouth, Canada) is a chromogenic assay for the determination of factor VIII (FVIII) coagulation activity in human plasma. Our objective was to characterize the performance of CRYO*check* Chromogenic Factor VIII on three different automated coagulation analyzers manufactured by Diagnostica Stago (STA-R Evolution), Siemens Healthineers (BCS XP) and Instrumentation Laboratory (ACL TOP CTS).

Methods

Precision was determined through a 20 day × 2 run × 2 replicate or a 5 day × 2 run × 2 replicate study using three reagent lots.

The reference interval was measured by testing 120 normal 3.2% citrated plasma samples with three reagent lots and calculated using a non-parametric method.

The limits of detection and quantification of the assay were determined by quantifying 8 congenital hemophilia A (HA) plasma samples in a 3 replicate × 5 day × 3 lot study design.

Assay performance was assessed relative to Coatest SP FVIII (Chromogenix/Instrumentation Laboratory, Bedford USA), in a method comparison study by testing 300+ normal and HA plasma samples on an IL ACL TOP. Sixty normal and HA samples were measured on each of the other two analyzer platforms and compared with the ACL TOP results.

Results

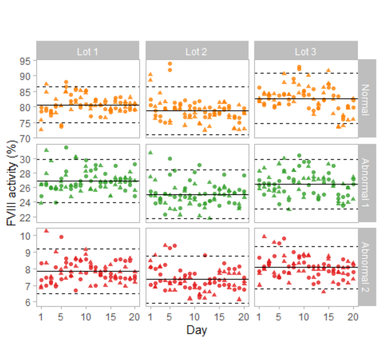
The assay total precision was <10% CV and the limits of detection and quantification were 0.5% (FVIII) on each of the three coagulation analyzers. The reference intervals were comparable across analyzers ranging from 43 to 164% FVIII. CRYO*check* Chromogenic Factor VIII and Coatest SP FVIII results on the IL ACL TOP were similar with a correlation (r^2) of >0.9 and a bias of <10% up to 150% FVIII activity. CRYO*check* Chromogenic Factor VIII results on the BCS and STA-R Evolution were comparable to the ACL TOP.

Conclusions

We observed excellent performance and consistency of CRYO*check* Chromogenic Factor VIII on three common coagulation analyzers when measuring precision, reference interval and limits of detection and quantification. Our findings also suggest that CRYO*check* Chromogenic Factor VIII performs comparably to another in-market chromogenic FVIII assay for the quantification of FVIII:C activity while offering compatibility with multiple analyzer platforms and a frozen format that expedites reagent preparation.

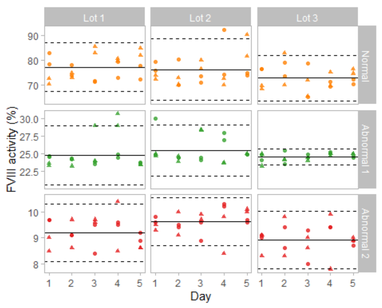
Results of a multi-day single site precision study using three lots of CRYO*check* Chromogenic FVIII to measure a normal and two abnormal plasma samples. The mean FVIII % result (solid black line) ± two standard deviations (dashed lines) are indicated in the figures while the means, repeatability and across lot reproducibility are reported in the corresponding tables.

On an ACL TOP



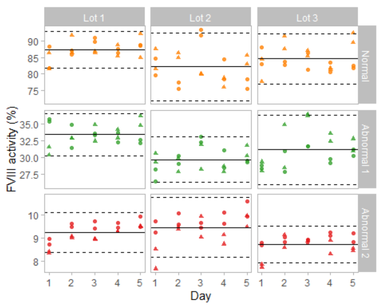
Control	N	Mean FVIII (%)	Repeatability		Reproducibility	
			SD	%CV	SD	%CV
Normal Plasma	240	80.8	3.3	4.1%	4.0	5.0%
Abnormal Plasma 1	240	26.1	1.5	5.6%	1.9	7.1%
Abnormal Plasma 2	240	7.8	0.7	8.4%	0.8	9.9%

On a BCS XP



Control	N	Mean FVIII (%)	Repeatability		Reproducibility	
			SD	%CV	SD	%CV
Normal Plasma	60	75.4	4.4	5.9%	6.3	8.4%
Abnormal Plasma 1	60	24.9	1.0	4.2%	1.7	7.0%
Abnormal Plasma 2	60	9.2	0.6	6.2%	0.7	7.2%

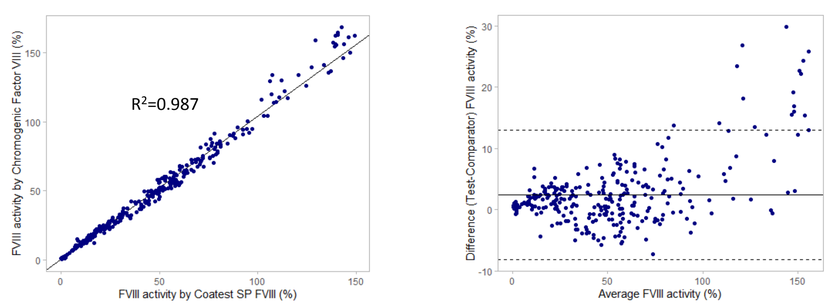
On a STA-R Evolution



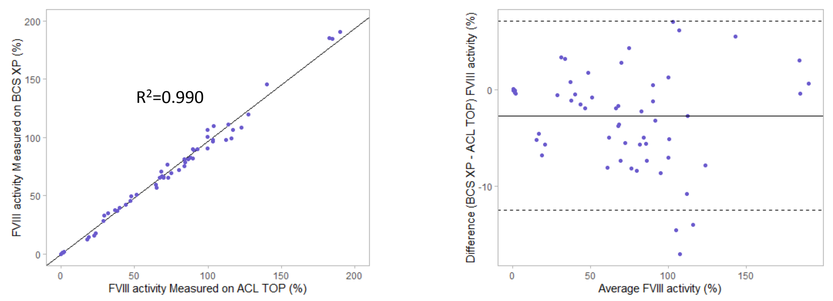
Control	N	Mean FVIII (%)	Repeatability		Reproducibility	
			SD	%CV	SD	%CV
Normal Plasma	60	84.8	2.7	3.2%	5.1	6.0%
Abnormal Plasma 1	60	31.4	1.4	4.5%	2.7	8.7%
Abnormal Plasma 2	60	9.1	0.3	2.9%	0.6	6.7%

Scatter and Bland- Altman plots showing the agreement between:

Coatest SP VIII and CRYO*check* Chromogenic Factor VIII on the ACL TOP (n=318)



CRYO*check* Chromogenic Factor VIII on the ACL TOP and BCS XP (n=60)



CRYO*check* Chromogenic Factor FVIII on the ACL TOP and the STA-R Evolution (n=60)