

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k102851

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Factor VIII activity

D. Type of Test:

Quantitative

E. Applicant:

r² Diagnostics, Inc.

F. Proprietary and Established Names:

NoFact VIII Deficient Plasma

G. Regulatory Information:

1. Regulation section:
21 CFR § 864.7290, Factor deficiency test
2. Classification:
Class II
3. Product code:
GJT, Plasma, Coagulation factor deficient
4. Panel:
81 Hematology

H. Intended Use:

1. Intended use(s):
NoFact VIII Deficient Plasma is a human plasma immunodepleted of Factor VIII and intended for the quantitative determination of Factor VIII activity in citrated plasma from patients suspected of FVIII deficiency. FVIII activity is based on the activated partial thromboplastin time. For in vitro diagnostic use.
2. Indication(s) for use:
Same as intended use
3. Special conditions for use statement(s):
For prescription use only
4. Special instrument requirements:
Diagnostica Stago STA family of analyzers.

I. Device Description:

NoFact VIII Deficient Plasma kit contains 10 x 1 mL vials of buffered and lyophilized human plasma immunodepleted of Factor VIII to contain less than 1% Factor VIII activity.

J. Substantial Equivalence Information:

1. Predicate device name(s):
STAGO VIII Deficient Plasma Kit
2. Predicate 510(k) number(s):
k892859
3. Comparison with predicate:

Similarities		
Item	Device: NoFact VIII Deficient Plasma (k102851)	Predicate: STAGO Deficient VIII (k892859)
Intended Use	NoFact VIII Deficient Plasma is a human plasma immunodepleted of Factor VIII and intended for the quantitative determination of Factor VIII activity in plasma.	Same
Measurement Principle	Clot-based Factor VIII activity assay using a modified activated partial thromboplastin time (APTT) test and Factor VIII deficient plasma.	Same
Closed vial storage	2 - 8°C	Same

Differences		
Item	Device: NoFact VIII Deficient Plasma (k102851)	Predicate: STAGO Deficient VIII (k892859)
Reconstituted stability	2-8°C: 8 hours Room temperature (18-26°C): 4 hours	On-board STA Compact® and STA-R®: 4 hours
Final Product Form	Kit contains 10 x 1 mL lyophilized vials	Kit containing 6 x 1 mL lyophilized vials

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2, Evaluation of Precision of Quantitative Measurement Methods; Approved Guidelines-Second Edition, 2004.

CLSI H21-A5, Collection, Transport and Processing of Blood Samples for Testing Plasma-based Coagulation Assays and Molecular Hemostasis Assays; Approved Guideline-Fifth Edition, 2008.

CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline, 2003.

L. Test Principle:

In the activated partial thromboplastin time (APTT), factor VIII deficient plasma provides normal activity for all procoagulants except for factor VIII. When normal plasma is added to factor VIII deficient plasma, the APTT reverts to normal. Factor VIII activity in a patient's plasma is determined by performing a modified activated partial thromboplastin time (APTT). Patient plasma is diluted and added to NoFact VIII Deficient Plasma. The APTT clotting time of this mixture is inversely proportional to factor VIII concentration (% activity) in the patient plasma.

M. Performance Characteristics:

1. Analytical performance:

a. *Precision/Reproducibility:*

Three lots of NoFact VIII Deficient Plasma were evaluated for precision using the Diagnostica Stago STA Compact® analyzer and Stago PTT Automate 5 reagent. Acceptance criteria were < 10% for within-run %CV and < 15% for within-device %CV. FVIII activity measurements of normal control plasma (System N) and abnormal control plasma (System P) were analyzed in duplicate for each run, with two runs per day, over a total of 20 days (n = 80

per lot). The calculated within-run %CV and within-device %CV met the acceptance criteria.

Sample Type	Mean FVIII activity, %	NoFact VIII Lot#	% CV Within-run	% CV Between-day	% CV Within-Device
System N (Normal Control Plasma)	91.6%	1	3.3	3.0	3.4
		2	4.7	3.0	3.9
		3	4.7	2.0	6.8
System P (Abnormal Control Plasma)	33.3%	1	5.9	4.6	5.8
		2	7.8	5.0	7.3
		3	6.4	3.5	8.1

b. *Linearity/assay reportable range:*

Linearity testing was performed using three lots of NoFACT VIII Deficient Plasma on the STA Compact® analyzer using Stago PTT Automate 5 reagent and Stago STA® Unicalibrator. A series of 11 FVIII concentrations ranging from 0.7% to 160% were created by reconstituting ISTH standard plasma and diluting with imidazole buffered saline. The FVIII dilutions were run in duplicate for each NoFACT VIII Deficient Plasma lot and the average activities were plotted against their assigned values. Acceptance criterion for allowable total nonlinearity was 15% and each lot of NoFACT VIII Deficient Plasma results were linear within the criterion. The results support the claimed assay reportable range of 1% - 160% FVIII activity. The calculated slope, intercept, and correlation coefficient are provided in the following table:

NoFact VIII Deficient Plasma	Slope	Intercept	r
Lot 1	1.055	0.3	0.99977
Lot 2	0.988	1.1	0.99961
Lot 3	1.04	-0.5	0.99941

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Real Time Stability: Three lots of NoFACT VIII Deficient Plasma were stored at 2-8 °C and at periodic times vials were reconstituted for stability testing. The study was performed on the STA Compact® using Stago PTT Automate 5 reagent to determine the recovery of FVIII activity for System N and System P controls. Real time stability was tested for 26, 28, and 33 months and all results were within the control acceptance range. Results for accelerated stability, which projects a 2.4 year shelf life, support a 2-year shelf life claim of NoFACT VIII Deficient Plasma when stored at 2-8 °C. Ongoing real-time stability testing will be used to update the shelf life.

Reconstituted Stability: Vials from 3 lots of NoFact VIII Deficient Plasma were reconstituted and stored at 2, 6, 8 and 24 hours at 2-8°C. An additional set of vials were stored at 2, 4, 6 and 8 hours at room temperature (18-26°C). The recovered FVIII activity values at the time of reconstitution were considered the "zero hour" baseline. At the time periods after reconstitution, vials from both sets of temperatures were run and the recovery at that time

point was determined. These recoveries were compared to the baseline recovery by calculating the % shift in value: (baseline value - time point value) divided by (baseline value). The criterion for acceptance was a shift of $\leq 10\%$. The data indicate that the % shift at each relevant time point tested met the specified limitation. Reconstituted NoFACT VIII Deficient Plasma is stable for 4 hours when stored at room temperature (18-26°C) and for 8 hours when stored at 2-8 °C.

- d. *Detection limit:*
Not applicable
 - e. *Analytical specificity:*
Interference studies were conducted by spiking pooled normal plasma (PNP) with various concentrations of hemoglobin, bilirubin, and triglycerides. Each PNP interferent dilution was then assayed for its FVIII activity on the STA Compact® using Stago PTT Automate 5 and NoFact VIII Deficient Plasma. The maximum concentration tolerated in the study was defined as the highest concentration of interferent wherein a shift relative to the recovered value of the unspiked PNP clotting time was less than 10%. Study results showed that factor VIII activity using NoFACT VIII Deficient Plasma is not affected by hemoglobin up to 500 mg/dL, unconjugated bilirubin up to 20 mg/dL, and triglycerides up to 2000 mg/dL.
 - f. *Assay cut-off:*
Not applicable
2. Comparison studies:
- a. *Method comparison with predicate device:*
A method comparison study was conducted at 3 sites using a combined total of 233 samples to compare the performance of the NoFact VIII Deficient Plasma to the predicate device (STA Deficient FVIII) using Stago PTT Automate 5 reagent on the STA Compact® analyzer. The study included apparently normal healthy donors and patients suspected of FVIII deficiency. The clinical distribution and demographic description of the 233 samples are detailed in the table below:

	Site 1	Site 2	Site 3
Total (n):	90	90	53
Normal donors:	45	40	43
Abnormal:	45	50	10
- Hemophilia	40	41	7
- Sepsis	2	2	2
- VWD	3	4	-
- Surgery	-	2	-
- Other	-	1	1

Gender	Sample size (n)	Age	Sample size (n)
Male	144	<21 yrs	30
Female	89	21-60 yrs	197
		>60 yrs	6

The method comparison study data analyses are included in the following table. Acceptance criteria were slope between 0.8 – 1.2 and a correlation coefficient (r) of > 0.9.

	All Sites (n = 233)	Site 1 (n = 90)	Site 2 (n = 90)	Site 3 (n = 53)
Slope (95% CI)	0.845 (0.825-0.865)	0.861 (0.844-0.878)	0.914 (0.891-0.936)	0.831 (0.777-0.884)
Intercept (95% CI)	4.2 (1.9-6.5)	2.8 (1.1-4.5)	2.5 (-0.1-5.1)	5.9 (-0.606-12.422)
r	0.984	0.995	0.993	0.976

- b. *Matrix comparison:*
Fresh vs. Once Thawed Samples – FVIII activity was tested on patient and donor samples using the Stago PTT Automate 5 reagent on the STA Compact® analyzer. Eighteen (18) patient samples (9 normal and 9 abnormal) were used for the study. After testing the fresh samples, samples were split and stored at -20°C and -80°C for one to three days. Each sample was then thawed and re-tested. Acceptance criterion was $r > 0.90$. Regression analysis produced a slope, intercept, and correlation coefficient (r) of 1.064, -0.02, and 0.994 respectively for the -20°C samples and a slope, intercept, and correlation coefficient (r) of 0.863, 0.02, and 0.998 respectively for the -80°C samples.
3. Clinical studies:
- Clinical Sensitivity:*
Not applicable
 - Clinical specificity:*
Not applicable
 - Other clinical supportive data (when a. and b. are not applicable):
Not applicable
4. Clinical cut-off:
Not applicable
5. Expected values/Reference range:
 Verification of the normal range for Factor VIII activity was performed using NoFact VIII Deficient Plasma. A total of 92 samples of apparently normal healthy donors were tested for Factor VIII activity with the Stago PTT Automate 5 reagent on the STA Compact® analyzer. Statistical analysis of the results verified the cited normal range for Factor VIII activity of 50 - 150% when using the NoFACT VIII Deficient Plasma.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.