

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

K043459

B. Purpose for Submission:

To seek clearance for HemosIL Factor XII Deficient Plasma designed for quantitative determination of factor XII activity on IL and ELECTRA Coagulation Systems.

C. Measurand:

Factor XII Deficient Plasma

D. Type of Test:

Quantitative clotting assay

E. Applicant:

Instrumentation Laboratory Company

F. Proprietary and Established Names:

HemosIL Factor XII Deficient Plasma

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7290

2. Classification:

Class II

3. Product code:

GJT

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

HemosIL Factor XII Deficient Plasma is intended for the quantitative determination of factor XII activity on IL and ELECTRA Coagulation Systems.

2. Indication(s) for use:
HemosIL Factor XII Deficient Plasma is human plasma immunodepleted of factor XII and intended for the *in vitro* diagnostic quantitative determination of factor XII activity in citrated plasma, based on the activated partial thromboplastin time (APTT) assay on IL Coagulation and ELECTRA Systems.
3. Special conditions for use statement(s):
Each laboratory should validate their choice of reagent/instrument combination.
4. Special instrument requirements:
IL Coagulation and ELECTRA Systems

I. Device Description:

HemosIL Factor XII Deficient Plasma is human plasma immunodepleted of factor XII and intended for the *in vitro* diagnostic quantitative determination of factor XII activity in citrated plasma based on the activated partial thromboplastin time (APTT) assay on IL Coagulation and ELECTRA Systems.

Abnormalities of the intrinsic pathway factors are determined by performing a modified activated partial thromboplastin time (APTT) test. Patient plasma is diluted and added to plasma deficient in factor XII. Correction of the clotting time of the deficient plasma is proportional to the concentration (% activity) of factor XII in the patient plasma, interpolated from a calibration curve.

J. Substantial Equivalence Information:

1. Predicate device name(s):
 - (a) Hemoliance Factor XII Deficient Plasma on the ELECTRA Series Analyzers
 - (b) HemosIL Factor XII Deficient Plasma on the ACL Family of Analyzers
2. Predicate 510(k) number(s):
 - (a) K893534
 - (b) K002400
3. Comparison with predicate:

Similarities			
Item	Device	Predicate	
	HemosIL Factor XII Deficient Plasma	(a) Hemoliance FXII Deficient Plasma on ELECTRA Analyzers	(b) HemosIL FXII Deficient Plasma on ACL Analyzers
Sample type	Citrated plasma	Same	Same
Storage conditions	Unopened: refrigerate	Same	Same

Similarities			
Item	Device	Predicate	
	2-8 °C until expired		

Differences			
Item	Device	Predicate	
Reagent	Lyophilized human plasma immunodepleted of FXII	Lyophilized human plasma congenitally deficient of FXII	Same as device
Stability after reconstitution	24 hours at 2-8°C or 24 hours at 15°C on the ACL Futura/ACL Advance Systems and ACL TOP	8 hours at 2-8°C	4 hours at 2-8°C

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

L. Test Principle:

In a well established testing method, patient plasma is diluted and added to plasma deficient in factor XII. Correction of the clotting time of the deficient plasma is proportional to the concentration (% activity) of factor XII in the patient plasma, interpolated from a calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A precision study was performed using two levels of control: HemosIL Normal Control and HemosIL Special Test Control Level 2. Each control was run in replicates of four twice a day for ten days (n=80) on four instruments. HemosIL APTT-SP (K973306) and HemosIL SynthASil (K953981) were used as the APTT reagents throughout testing (combinations below).

ACL 9000 + APTT-SP
 ACL Futura + APTT-SP
 ACL TOP + SynthASil
 ELECTRA 1600C + SynthASil

Within run, between run, and total % CV were calculated according to NCCLS Document EP5-T2.

HemosIL Normal Control: Mean % activity of factor XII for all combinations was 100%, within run 3.3%CV, between run 4.3% CV and total precision

5.6% CV.

HemosIL Special Test Control Level 2: Mean % activity of factor XII for all combinations was 33%, within run 3.6%CV, between run 3.7% CV and total precision 5.3% CV.

Acceptance Criteria:

	Normal	Special Test Level 2
Within run	≤ 10%	≤ 15%
Between Run	≤ 12%	≤ 17%

Additional studies for HemosIL Factor XII Deficient Plasma were performed on the other members of the ACL and ELECTRA coagulation families. On each instrument HemosIL Normal Control and HemosIL Special Test Control Level 2 were run in replicates of four twice a day for five days (n=40). Testing was performed using APTT-SP and SynthASil as the APTT reagents (combinations below).

ACL 300 + APTT-SP
 ACL 3000 + APTT-SP
 ACL Advance + APTT-SO
 ELECTRA 1400C + SynthASil
 ELECTRA 1800C + SynthASil

HemosIL Normal Control: Mean % activity of factor XII for all combinations was 99%, within run 3.3%CV, between run 4.1% CV and total precision 5.5% CV.

HemosIL Special Test Control Level 2: Mean % activity of factor XII for all combinations was 33%, within run 3.6%CV, between run 3.8% CV and total precision 5.4% CV.

b. Linearity/assay reportable range:

Not assessed

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

Stability:

Reconstituted stability testing was performed to support the following package insert claims of 24 hours at 2-8°C for the new HemosIL Factor XII Deficient Plasma.

Vials of HemosIL Factor XII Deficient Plasma were opened, tested at time 0 and stored at 2-8°C for the duration of testing. HemosIL Normal Control (K021023) and HemosIL Special Test Control Level 2 (K040359) were each tested in quadruplicate on an ACL 300 at the time intervals 0, 2, 4, 8, 24, and

27 hours. HemosIL APTT-SP (K973306) was used as the APTT reagent throughout testing.

Acceptance Criteria:

1. HemosIL Normal Control: $\pm 10\%$ change from the mean at time zero
2. HemosIL Special Test Control Level 2: $\pm 10\%$ change from the mean at time zero

The data supports that HemosIL Factor XII Deficient Plasma is stable for 24 hours at 2-8°C in the original vial.

d. Detection limit:

Not applicable

e. Analytical specificity:

The HemosIL Factor XII Deficient Plasma product insert refers customers to the specific reagent inserts for relative interference claims since interference is dependent on the individual activated partial thromboplastin time reagent used. The product insert also states that samples with excessive hemolysis, icterus or lipemia should not be used.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

An in-house method comparison study was performed at Instrumentation Laboratory's (IL) facilities in Orangeburg, NY and one additional field site. Data compared the performance of the new HemosIL Factor XII Deficient Plasma versus HemosIL Factor XII Deficient Plasma on an ACL 3000, ACL 10000, ACL Advance and ACL TOP and versus Hemoliance Factor XII Deficient Plasma on an ELECTRA 1600C. The study evaluated approximately 70 citrated plasma samples, each run in duplicate.

HemosIL APTT-SP (K973306) and HemosIL SynthASil (K953981) were used as the APTT reagents throughout testing. A clinical breakdown of the abnormal patient samples obtained from CliniSys Associates in Atlanta, GA is as follows:

Sample Quantity	ACL 3000	ACL 10000	ACL Advance	ACL TOP	ELECTRA 1600C
Normal	31	30	30	30	34
High FXII/Renal Failure	14	12	12	12	15
DIC	12	13	13	15	12
Low FXII	14	16	15	15	12

Samples were run in duplicate and the means of the reference and test devices were used to calculate the correlation statistics. To show that there is no variation between the mean results and singlet testing, the correlation data were also calculated using the first replicate of the new test versus the first replicate of the predicate test.

All method comparisons met the sponsor's acceptance criteria for slope (0.85-1.15) and correlation (≥ 0.95). The mean r value for all ACL family instrument/reagent combinations is 0.971. The results of running the new HemosIL Factor Deficient Plasma versus the predicate device (Hemoliance Factor XII Deficient Plasma) on an ELECTRA 1600C using HemosIL SynthASil show a correlation of 0.986.

Field Site Study:

At the South-East Regional Health Authority, Moncton, Canada, a method comparison study of the new HemosIL Factor XII Deficient Plasma versus the predicate device HemosIL Factor XII Deficient Plasma was conducted on an ACL Futura using 60 citrated patient plasma samples (30 normal and 30 abnormal hemostasis samples). Patient samples were run in duplicate for both the predicate and the new deficient plasmas. HemosIL APTT-SP (K973306) was used as the APTT reagent throughout testing.

The results from running HemosIL Factor XII Deficient Plasma versus the predicate device on an ACL Futura show a correlation of 0.974, which meets the sponsor's correlation acceptance criteria of ≥ 0.95 .

b. Matrix comparison:
Not applicable

3. Clinical studies:

a. Clinical Sensitivity:
Not applicable

b. Clinical specificity:
Not applicable

- c. Other clinical supportive data (when a. and b. are not applicable):

Reagent Comparison:

A reagent comparison study was conducted at Instrumentation Laboratory's facility in Orangeburg, NY, to demonstrate the equivalent performance of HemosIL Factor XII Deficient Plasma with various APTT reagents on representative IL instruments. Testing was conducted on 56 citrated plasma samples (25 normal and 31 abnormal with the following instrument/reagent combinations:

ACL 6000 + SynthASil
ACL 6000 + SynthAFax
ELECTRA 1400C + SynthAFax

The mean of the correlation of the instrument/reagent combinations ($r=0.972$) is within the sponsor's acceptance criteria of ≥ 0.95 .

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The sponsor cited age-related references values in Wintrobe's Clinical Hematology, Tenth Edition, Vol. 2, 1999: p1575t, ISBN 0-683-18242-0.

The product insert reports expected values of 50-150% factor XII activity and further advises each laboratory to establish its own normal range due to many variables which may affect clotting times (including the population age).

N. Proposed Labeling:

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

O. Conclusion:

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