

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

**A. 510(k) Number:**

#K040843

**B. Purpose for Submission:**

New device

**C. Analyte:**

Von Willebrand Factor (vWF)

**D. Type of Test:**

Quantitative

**E. Applicant:**

Instrumentation Laboratory Co.

**F. Proprietary and Established Names:**

IL HemosIL vWF Activity Kit; vWF Deficiency Test

**G. Regulatory Information:**

1. Regulation section:  
CFR Section 864.7290 – Factor Deficiency Test
2. Classification:  
Class II
3. Product Code:  
GGP – Quantitative Factor Deficiency Test
4. Panel:  
Hematology (81)

**H. Intended Use:**

1. Intended use(s):  
The IL HemosIL vWF Activity Kit is an in vitro diagnostic automated latex enhanced immunoturbidometric assay for the quantitative determination of vWF activity in human citrated plasma on IL Coagulation Systems.
2. Indication(s) for use:  
Same as above
3. Special condition for use statement(s):  
N/A
4. Special instrument Requirements:  
IL Coagulation Systems (ACL 8000, 9000, and 10000 Analyzers)

**I. Device Description:**

The HemosIL vWF Activity Kit is a latex particle enhanced immunoturbidometric assay to quantify vWF activity in plasma. It consists of (1) a lyophilized suspension of polystyrene latex particles coated with purified anti-vWF mouse monoclonal antibody directed against a functional epitope of vWF, containing bovine serum albumin (BSA), stabilizers and preservative; and (2) Tris buffer containing BSA, stabilizers and preservative.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Shield Diagnostics, Ltd. vWF Activity ELISA; Dade Behring BC vWF:RCofactor Activity Reagent
2. Predicate K number(s):  
#K000398; #K972116
3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Methodology	Immunoassay	Same
Monoclonal antibody origin	Hybridoma cell line, RFF-VIII:R/1	Same
Calibration standard traceability	NIBSC WHO/ECBS 4 <sup>th</sup> International Std. for FVIII/vWF Activity in Plasma (Code: 97/586)	Same
Sample type	Citrated plasma	Same
Stability	2° - 8° C.	Same
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Test principle	Latex agglutination enhanced immunoturbidometry (ITA)	Enzyme-linked immunosorbency (ELISA)
Detection limit	12.0%	1.6%

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

IFCC Approved Recommendation (1987) on the Theory of Reference Values; NIBSC WHO/ECBS 4<sup>th</sup> International Standard for Factor VIII and vWF in Plasma (Code: 97/586); NCCLS EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline (1999); and NCCLS H21-A3: Collection, Transport and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays; Approved Guideline-4<sup>th</sup> Edition (2003).

**L. Test Principle:**

The HemosIL vWF Activity Kit uses a specific anti-vWF monoclonal adsorbed onto the latex reagent and directed against the platelet binding site of vWF (glycoprotein Ib receptor). When it reacts with the vWF in patient plasma, the degree of agglutination is directly proportional to the activity of vWF activity in the sample, and is determined by measuring the decrease in transmitted light caused by the aggregates.

**M. Performance Characteristics (if/when applicable):**1. Analytical performance:*a. Precision/Reproducibility:*

Testing was performed on the ACL 9000, using duplicates of (3) levels of controls (N=84), each, according to NCCLS EP5-A Protocol. The HemosIL Normal Control had a mean of 79.6%; the Level 1, a mean of 49.8%; and the Level 2, a mean of 27.7%. They all met the acceptance criteria with %CV's ranging from 1.7 – 9.0%.

*b. Linearity/assay reportable range:*

Reagent, (3) lots and (5) replicates of Calibration Plasma/Factor Diluent were used in dilutions to obtain the assay range. Reported values vs expected values yielded R2 values ranging 0.9845 – 0.9941. The activity (%) ranged 19.4 – 275.5 to support the claim of 21 – 200%.

*c. Traceability (controls, calibrators, or method):*

Value assignment was made from multiple runs against a house standard traced to the NIBSC WHO/ECBS 4<sup>th</sup> International Standard for FVIII/vWF Activity in Plasma (Code :97/586).

*d. Detection limit:*

Replicates (10), of (3) lots of reagent, diluted with Diluent, yielded 12.2% (the greater of the mean + 2SD).

*e. Analytical specificity:*

Pooled normal and abnormal plasmas, (2) each, were spiked with varying levels of interferents, bilirubin and lipids. Bilirubin, at 3.8 mg/dL, and lipids, at 265 mg/dL, met the acceptance criteria of  $\pm 15\%$  recovery of the unspiked value.

*f. Assay cut-off:*

N/A

2. Comparison studies:a. *Method comparison with predicate device:*

The company provided an in-house comparison study, performed on the ACL 9000, using citrated samples (N=108) obtained from (3) hospitals. Samples ranged from 0 – 192% vWF activity. HemosIL vs Shield Diagnostics vWF Activity ELISA yielded these values:

$$r = 0.9723; S = 0.832; I = 4.782$$

Duplicate vs singlet testing was also performed, and yielded values, as follows, to demonstrate no significant difference between the two:

$$r = 0.9710; S = 0.849; I = 4.207$$

b. *Matrix comparison:*

N/A

3. Clinical studies:a. *Clinical sensitivity:*

N/A

b. *Clinical specificity:*

N/A

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

The company also provided a clinical comparison of the HemosIL Reagent vs a reference assay, Dade Behring BC vWF:RCo Reagent. Duplicate testing of samples (N = 114) was performed on the ACL 9000 at the Coagulation Lab in Hamburg, Germany. Samples ranged from 0 – 213% vWF activity. They yielded values of:

$$r = 0.9497; S = 0.8406; I = 9.7557$$

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

Using IFCC guidelines for determining reference values, the company tested healthy blood donors (N = 248) from the Hospital Vall d'Hebron in Barcelona, Spain. Type "O" (N = 122), with M = 51 and F = 71; and Types "A", "B" and "AB" (N = 126), with M = 59 and F = 67 yielded the following results:

	<b>Type "O"</b>		<b>Other types</b>	
	<u>95% Limit</u>	<u>90% C.I.</u>	<u>95% Limit</u>	<u>90% C.I.</u>
Lower	38.03	34.65 – 41.05	49.19	47.55 – 57.85
Upper	125.24	116.00 - 142.50	169.71	156.50 – 182.50

**N. Conclusion:**

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