

HEMOSIL[®]

D-DIMER



D-DIMER

Simple, Proven and Efficient,
for the Exclusion of VTE

D-Dimer in Clinical Practice



In the Diagnosis of DVT and PE

Diagnosis of Venous Thromboembolism (VTE), which includes Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE), often begins with a clinical evaluation, followed by D-Dimer testing. Confirmatory tests generally involve imaging techniques. For DVT, these are lower-limb venous Compression Ultrasonography (CUS) and venography, which is invasive and considered the gold standard. For PE, imaging tests are Computerized Tomography (CT) scanning or ventilation/perfusion (V/Q) lung scanning and angiography, which are also invasive.

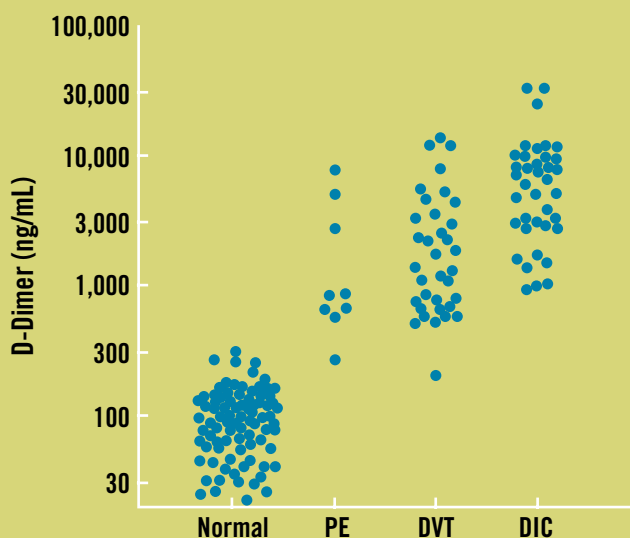
A substantial number of recent publications report the use of D-Dimer, together with a pre-test probability (PTP) assessment, as a safe, cost-effective management strategy for the evaluation of patients presenting with clinically-suspected VTE. This approach allows DVT and/or PE to be ruled out in outpatients with suspected VTE who have a low or low-moderate PTP and a negative D-Dimer, reducing the number of imaging tests required, particularly invasive ones.

Other Clinical Applications

D-Dimer testing has been evaluated in a number of clinical applications, such as predictive factors, for recurrences of VTE after discontinuation of oral anticoagulant therapy and as an indicator of pregnancy complications.^{1,2} Other studies suggest that elevated D-Dimer levels in the normal population may indicate the risk for thrombosis.³

D-Dimer testing is also included in recent definitions of clinical laboratory criteria for the diagnosis and staging of Disseminated Intravascular Coagulation (DIC).⁴

D-DIMER LEVELS IN VTE AND DIC PATIENT GROUPS VS. NORMAL SUBJECTS



In patients with PE, DVT and DIC, D-Dimer levels are > 230 ng/mL D-Dimer Units (D-DU).

HemosIL D-Dimer

D-Dimer is a fully automated, latex-enhanced immunoassay for the exclusion of VTE in outpatients suspected of DVT and PE, in conjunction with a clinical PTP assessment model. It quantitatively determines the amount of D-Dimer in human citrated plasma across IL Hemostasis systems.

The latex reagent is a suspension of polystyrene latex particles of uniform size, coated with a monoclonal antibody, highly specific for the D-Dimer domain included in fibrin degradation products or derivatives.

SAVES TIME AND RESOURCES

Optimizes laboratory workload

- Fully automated
- Same cut-off for the exclusion of DVT and PE throughout the entire ACL instrument line

Provides rapid patient response

- Results in < 7 minutes

ENHANCES PATIENT CARE

FDA-cleared for the exclusion of VTE with superior accuracy and precision

- Excellent Negative Predictive Value (NPV):
 - 100% for DVT and PE on ACL TOP® Family
 - 100% for DVT and 99.1% for PE on ACL ELITE® Systems
- Lower 95% CI limit < 95% for NPV of Low and Moderate PTP group
- In conjunction with a PTP score, excludes DVT and PE, using a cut-off value of 230 ng/mL D-DU

D-Dimer, with a PTP score, Safely Excludes DVT and PE

Using a cut-off of 230 ng/mL D-DU, D-Dimer successfully excluded DVT and PE in over 900 patients (two clinical studies) with an NPV of 100% and Sensitivity of 100%.

SINGLE-CENTER MANAGEMENT STUDY			
		ACL TOP	ACL 9000
VTE	Samples (n)	294	297
	NPV (%)	100	100
	Specificity (%)	36	38

MULTI-CENTER MANAGEMENT STUDY			
		ACL TOP	ACL 9000
DVT	Samples (n)	302	298
	NPV (%)	100	100
	Specificity (%)	41.6	33.8
PE	Samples (n)	330	331
	NPV (%)	100	99.1
	Specificity (%)	29.3	41.3

For more detail, see management studies section, under this page.

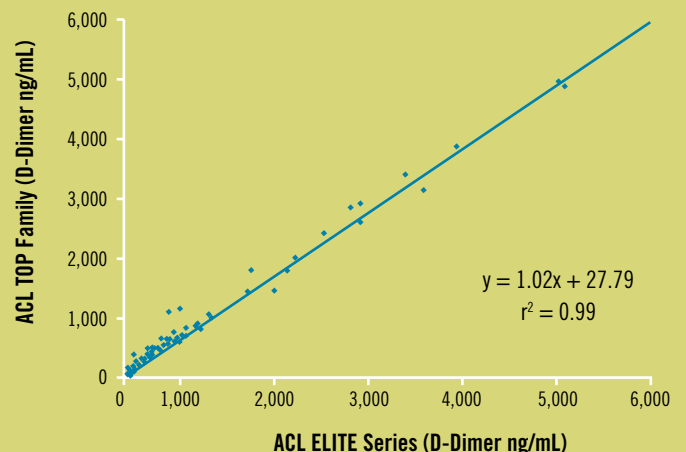
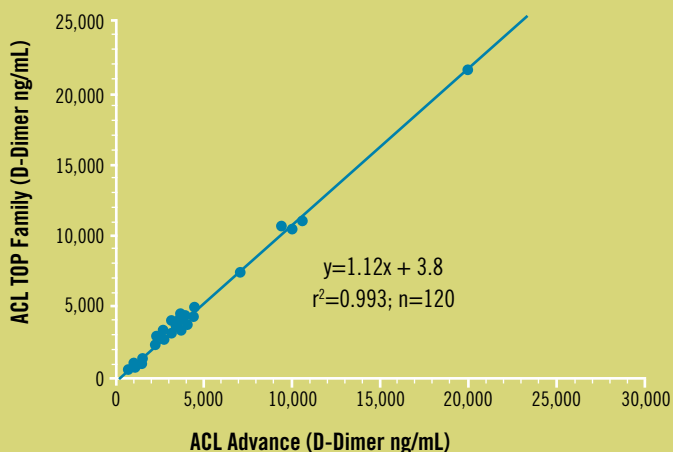
Analytical Performance on IL Hemostasis Systems

Linearity	Up to 1,050 ng/mL D-DU without rerun Up to 5,250 ng/mL D-DU with automated rerun			
Precision		Mean (ng/mL D-DU)	% CV (Total)	
ACL Family	Plasma pool	246	11.7	
	Low D-Dimer control	310	7.18	
	High D-Dimer control	732	2.99	
ACL Advance	Low D-Dimer control	304	13.58	
	High D-Dimer control	813	4.94	
ACL TOP Family	Plasma pool	282	9.0	
	Low D-Dimer control	340	7.7	
	High D-Dimer control	729	4.5	
Detection Limit				
ACL Family	140 ng/mL			
ACL Advance	156 ng/mL			
ACL TOP Family	69 ng/mL			
Interferences	ACL Advance/ACL Family	ACL TOP Family		
	<i>none up to:</i>	<i>none up to:</i>		
Hemoglobin	50 mg/dL	100 mg/dL		
Bilirubin	5 mg/dL	10 mg/dL		
Triglycerides	1,000 mg/dL	1,500 mg/dL		
Stability of Reconstituted Reagent				
Latex Reagent and Buffer	1 month at 2-8°C			
Calibrator	3 days at 15-25°C, 1 month at 2-8°C, 2 months at -20°C			
Onboard Stability	ACL 7000	ACL ELITE/ELITE PRO/8/9/10000	ACL Advance	ACL TOP Family
Latex Reagent	6 hrs at 15°C	1 day at 15°C	1 week at 15°C	2 days at 15°C
Reaction Buffer	6 hrs at 15-25°C	1 day at 15-25°C	1 week at 15°C	2 days at 15°C

METHOD COMPARISON

Excellent correlation

A comparison study of HemosIL D-Dimer on ACL TOP Family vs. ACL Advance, and on ACL TOP Family vs. ACL ELITE/ELITE PRO, using samples from outpatients suspected of VTE, demonstrated excellent correlation and slope.



VTE Management Studies with HemosIL D-Dimer

Single-Center Management Study

Enhancing Diagnosis of DVT and PE

An outcome study was performed on approximately 300 frozen samples from patients suspected of PE or DVT (26% frequency of VTE).

Positive samples were confirmed through standard imaging techniques. Results, below, are based on a cut-off value of 230 ng/mL D-DU.

VTE PERFORMANCE	D-DIMER ON ACL TOP	D-DIMER ON ACL 9000
Samples (n)	294	297
Sensitivity (%) (95% CI)	100 (95.1 - 100)	100 (95.2 - 100)
Specificity (%) (95% CI)	36 (29.6 - 42.6)	38 (31.4 - 44.6)
NPV (%) (95% CI)	100 (95.4 - 100)	100 (95.7 - 100)

Multi-Center Management Study

Excluding DVT and PE

A multi-center management study was performed at four hospitals with samples from patients suspected of PE and DVT. Patient management was based on a study-specific diagnostic algorithm, involving PTP scoring. DVT and PE patients were confirmed through standard imaging techniques.

Negative patients were confirmed at a three-month follow-up. Results, below, are based on a cut-off value of 230 ng/mL D-DU for the ACL TOP and ACL ELITE.

ACL TOP	DVT PERFORMANCE			PE PERFORMANCE		
	ALL SAMPLES	HIGH PTP	LOW+MODERATE PTP	ALL SAMPLES	HIGH PTP	LOW+MODERATE PTP
Samples (n)	302	53	249	330	24	306
Sensitivity (%) (95% CI)	100 (59/59) (93.9 - 100)	100 (27/27) (87.2 - 100)	100 (32/32) (89.1 - 100)	100 (50/50) (92.9 - 100)	100 (7/7) (59.0 - 100)	100 (43/43) (91.8 - 100)
Specificity (%) (95% CI)	41.6 (101/243) (35.3 - 48.0)	34.6 (9/26) (17.2 - 55.7)	42.4 (92/217) (35.7 - 49.3)	29.3 (82/280) (24.0 - 35.0)	17.6 (3/17) (3.8 - 43.4)	30.0 (79/263) (24.6 - 36.0)
NPV (%) (95% CI)	100 (101/101) (96.4 - 100)	100 (9/9) (66.4 - 100)	100 (92/92) (96.1 - 100)	100 (82/82) (95.6 - 100)	100 (3/3) (29.2 - 100)	100 (79/79) (95.4 - 100)

ACL ELITE

Samples (n)	289	54	244	331	25	306
Sensitivity (%) (95% CI)	100 (61/61) (94.1 - 100)	100 (29/29) (88.1 - 100)	100 (32/32) (89.1 - 100)	98.0 (49/50) (89.4 - 99.9)	100 (8/8) (63.1 - 100)	97.6 (41/42) (87.4 - 99.9)
Specificity (%) (95% CI)	33.8 (80/237) (27.8 - 40.2)	24.0 (6/25) (9.4 - 45.1)	34.9 (74/212) (28.5 - 41.7)	41.3 (116/281) (35.5 - 47.3)	41.2 (7/17) (18.4 - 67.1)	41.3 (109/264) (35.3 - 47.5)
NPV (%) (95% CI)	100 (80/80) (95.5 - 100)	100 (6/6) (54.1 - 100)	100 (74/74) (95.1 - 100)	99.1 (116/117) (95.3 - 100)	100 (7/7) (59.0 - 100)	99.1 (109/110) (95.0 - 100)

D-Dimer Kit Composition

PRODUCT	PART NUMBER	KIT CONFIGURATION
D-Dimer	0020008500	4 x 3 mL Latex Reagent (lyo) 4 x 9 mL Reaction Buffer (liq) 2 x 1 mL Calibrator (lyo)
D-Dimer Controls	0020008610	5 x 1 mL Low D-Dimer control (lyo) 5 x 1 mL High D-Dimer control (lyo)

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Additional Literature

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- Villa *et al.* Quantification of D-dimer using a new fully automated assay: its application for the diagnosis of deep vein thrombosis. *Haematologica*; 2000, 85:520-524.
- Wells *et al.* Evaluation of D-Dimer in the Diagnosis of suspected deep-vein thrombosis. *N Eng J Med* 2003; 349: 1227-35.

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