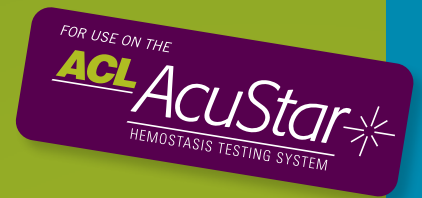


HEMOSIL® ACUSTAR

ANTIPHOSPHOLIPID ASSAY PANEL



Full automation for Antiphospholipid Syndrome diagnosis.

- ▶ HemosIL AcuStar Anti-Cardiolipin IgG
- ▶ HemosIL AcuStar Anti-Cardiolipin IgM
- ▶ HemosIL AcuStar Anti- β_2 Glycoprotein-I IgG
- ▶ HemosIL AcuStar Anti- β_2 Glycoprotein-I IgM

ANTIPHOSPHOLIPID SYNDROME

For the first time, full automation for faster, more accurate results.

- Cartridge-based, ready-to-use, precalibrated assays for unmatched simplicity
- Extended, six-week onboard stability—optimal for analysis 24 hours/day, 7 days/week
- Highly sensitive, chemiluminescent immunoassays offer superior accuracy and precision
- Extremely wide linearity ranges, with and without rerun
- Clinically validated 20 U/mL cutoff for all assays
- Uses serum or citrated plasma samples



What is Antiphospholipid Syndrome (APS)?

APS (also known as Hughes Syndrome) is an autoimmune disorder in which antiphospholipid antibodies are associated with venous and arterial thrombosis, recurrent fetal loss, repeated unexplained spontaneous abortion, or premature birth. APS occurs when autoantibodies are generated against phospholipid-binding proteins, such as β_2 Glycoprotein-I, and phospholipids, such as Cardiolipin. However, Prothrombin, Phosphatidyl Serine, Annexin V, Protein C, and Protein S have also been implicated.

APS can be classified as Primary APS (PAPS) or Secondary APS (SAPS). While PAPS occurs unrelated to any existing disease, SAPS occurs in conjunction with other autoimmune diseases,

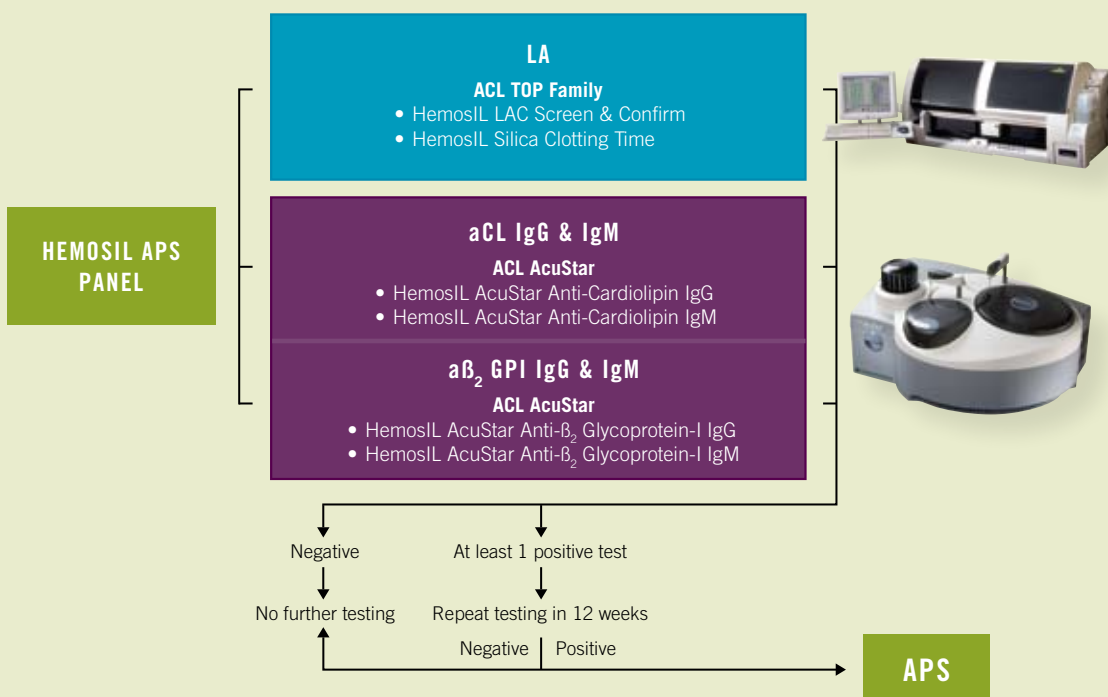
such as Systemic Lupus Erythematosus (SLE). Catastrophic APS is a rare, often fatal, condition involving thrombosis which leads to rapid organ failure.

A diagnosis of APS requires the presence of at least one clinical criteria and one laboratory criteria. The laboratory criteria are based on the presence of: Lupus Anticoagulant (LA), Anti-Cardiolipin (aCL), or Anti- β_2 Glycoprotein-I antibodies (a β_2 GPI). With a confirmed APS diagnosis, the physician is able to use clinical management strategies, such as lifelong anticoagulant therapy, to provide the patient with the most relevant and highest quality of care.

APS diagnosis requires the presence of one clinical criteria and one laboratory criteria.

CLINICAL CRITERIA	LABORATORY CRITERIA
<p>1. Vascular thrombosis (arterial, venous)</p> <p>2. Pregnancy morbidity</p> <ul style="list-style-type: none"> Unexplained fetal death beyond 10th week Premature birth before 34th week Three or more unexplained spontaneous abortions before 10th week 	<p>1. LA antibodies</p> <ul style="list-style-type: none"> Two occasions, at least 12 weeks apart <p>2. aCL antibodies</p> <ul style="list-style-type: none"> Medium or high titer of IgG and/or IgM Two occasions, at least 12 weeks apart <p>3. aβ_2GPI antibodies</p> <ul style="list-style-type: none"> IgG and/or IgM Two occasions, at least 12 weeks apart

Automated assays for aPL and LA antibodies integrate the ACL AcuStar™ and ACL TOP® Family of analyzers



Excellent analytical performance

Imprecision	Within Run % CV	Total % CV
Below cutoff	< 8	< 12
Medium titer	< 5	< 8
High titer	< 7	< 7

	aCL IgG	aCL IgM	aβ ₂ GPI IgG	aβ ₂ GPI IgM
Linearity (U/mL)	<i>Without Rerun</i> 2.4 – 2,024	<i>Without Rerun</i> 0.66 – 774	<i>Without Rerun</i> 6.3 – 6,100	<i>Without Rerun</i> 0.24 – 841
	<i>With Rerun</i> 2.4 – 40,480	<i>With Rerun</i> 0.66 – 15,480	<i>With Rerun</i> 6.3 – 122,000	<i>With Rerun</i> 0.24 – 16,820
Detection Limit (U/mL)	0.51	0.09	1.07	0.08
Cutoff (U/mL)	20	20	20	20

Clinical performance

Frozen citrated plasma samples were collected by a hospital laboratory specializing in the diagnosis of APS.

APS-confirmed patient samples included selected individuals diagnosed as:

- Primary APS (PAPS)
- Secondary APS (SAPS)

The control group of samples included:

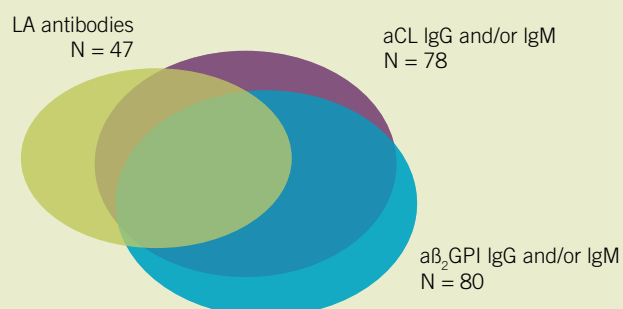
- Apparently healthy donors (Normal)
- Systemic Lupus Erythematosus (SLE) with no APS
- SLE-like
- Other autoimmune cardiovascular disorders (Other)

The samples were blind tested with the HemosIL AcuStar aPL assays. The table below illustrates the percentage of samples with a result above the cutoff (20 U/mL) and the aPL Panel subgroup indicates the percentage of positive samples when the results of at least one of the four assays were above the cutoff. The results indicate an excellent sensitivity and specificity for APS.

GROUP	APS		CONTROL			
	PAPS	SAPS	Normal	SLE	SLE-like	Other
N	23	69	103	115	5	6
aCL IgG (%)	56.5	53.6	0	7.8	0	16.7
aCL IgM (%)	34.8	33.3	1.0	8.7	0	16.7
aβ ₂ GPI IgG (%)	60.9	65.2	0	17.4	0	16.7
aβ ₂ GPI IgM (%)	30.4	29.0	0	8.7	0	16.7
aPL Panel (%)	69.6	72.5	1.0	21.7	0	16.7

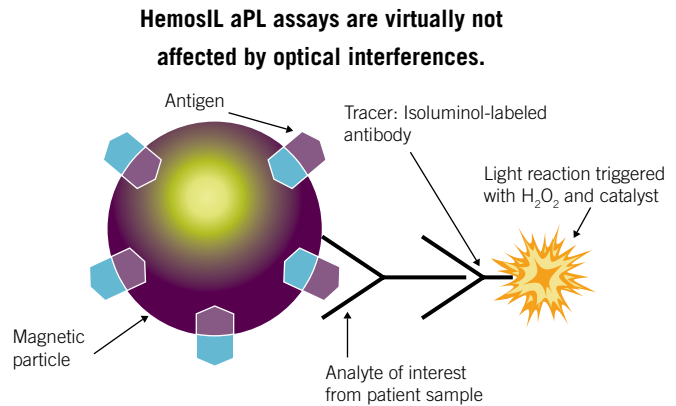
The HemosIL APS panel: maximizes efficiency in APS diagnosis

Samples from patients with PAPS and SAPS were positive for one or more of the aPL antibodies: LA antibodies, aCL IgG and/or IgM antibodies and aβ₂GPI IgG and/or IgM antibodies, as shown. This clearly indicates that a comprehensive testing panel maximizes efficiency in APS diagnosis.



Principle of the assays

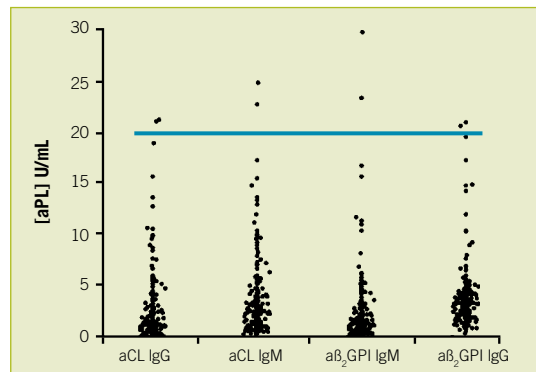
The components of the HemosIL AcuStar aPL assay panel are fully automated immunoassays, based on chemiluminescence technology. Magnetic particles are coated with human β_2 GPI, alone, (a β_2 GPI antibodies assays) and Cardiolipin, complexed with human β_2 GPI (aCL antibodies assays). The antigen-coated magnetic particles capture the aPL antibodies IgG and/or IgM, if present in the sample. An isoluminol-labeled secondary antibody in the tracer then binds to the captured antibodies; resulting in an emission of light proportionate to the concentration of the antibodies.



Standardization of the assays

A normal range study was performed using 252 citrated plasma samples from healthy donors*. All four aPL assays were standardized to a cutoff of 20 U/mL. HemosIL AcuStar aPL assays can be correlated with the chimeric antibody, HCAL, and the monoclonal antibody, EY2C9.

*Based on the 99th percentile as recommended by the Lupus Anticoagulant/Phospholipid-Dependent Antibodies ISTH subcommittee.



Standardization of Assays

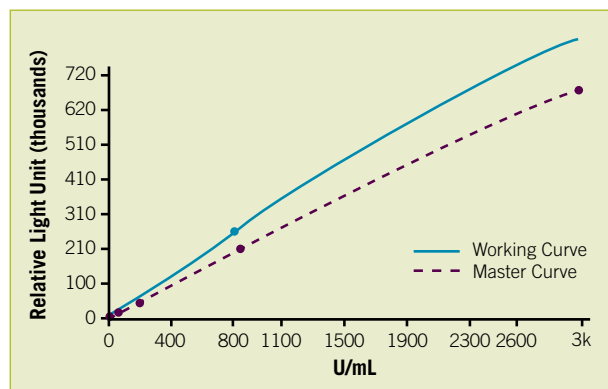
Calibration of the assays

Master Curve

- Predefined
- Lot-specific
- Imported into ACL AcuStar software via cartridge barcode

Working Curve

- Calibration-specific
- Performed on-site with Calibrators 1 & 2 in triplicate
- Once per lot



Calibration of Assays

Kit configurations

REAGENTS	PART NUMBER	KIT CONFIGURATION
HemosIL AcuStar Anti-Cardiolipin IgG	0009802004	1 Cartridge (50 tests) Anti-Cardiolipin IgG Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
HemosIL AcuStar Anti-Cardiolipin IgM	0009802008	1 Cartridge (50 tests) Anti-Cardiolipin IgM Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
HemosIL AcuStar Anti- β_2 Glycoprotein-I IgG	0009802012	1 Cartridge (50 tests) Anti- β_2 Glycoprotein-I IgG Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
HemosIL AcuStar Anti- β_2 Glycoprotein-I IgM	0009802016	1 Cartridge (50 tests) Anti- β_2 Glycoprotein-I IgM Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
CONTROLS	PART NUMBER	KIT CONFIGURATION
HemosIL AcuStar Anti-Cardiolipin IgG Controls	0009802104	Low Anti-Cardiolipin IgG Control, 3 x 1 mL (liq) High Anti-Cardiolipin IgG Control, 3 x 1 mL (liq)
HemosIL AcuStar Anti-Cardiolipin IgM Controls	0009802108	Low Anti-Cardiolipin IgM Control, 3 x 1 mL (liq) High Anti-Cardiolipin IgM Control, 3 x 1 mL (liq)
HemosIL AcuStar Anti- β_2 Glycoprotein-I IgG Controls	0009802112	Low Anti- β_2 GPI IgG Control, 3 x 1 mL (liq) High Anti- β_2 GPI IgG Control, 3 x 1 mL (liq)
HemosIL AcuStar Anti- β_2 Glycoprotein-I IgM Controls	0009802116	Low Anti- β_2 GPI IgM Control, 3 x 1 mL (liq) High Anti- β_2 GPI IgM Control, 3 x 1 mL (liq)

References

- Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. *N Engl J Med* 2002;346(10):752-763
- Hanly JG. Antiphospholipid syndrome: an overview. *CMAJ* 2003;168(13):1675-82
- Galli M. Antiphospholipid syndrome: associate between laboratory tests and clinical practice. *Pathophysiol Haemost Thromb* 2003/2004; 33:249-255
- Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RH, de Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A, Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS), *J Thromb Haemost.* 2006;4(2): 295-306

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