HEMOSIL® ACUSTAR

ANTIPHOSPHOLIPID ASSAY PANEL

Full automation for APS investigation



FOR USE ON THE ACL AcuStar HEMOSTASIS TESTING SYSTEM

- **HemosIL AcuStar Anti-Cardiolipin IgG**
- **HemosIL AcuStar Anti-Cardiolipin IgM**
- **HemosIL AcuStar Anti-ß$_2$ Glycoprotein-I IgG**
- **HemosIL AcuStar Anti-ß$_2$ Glycoprotein-I IgM**

NEW

- **HemosIL AcuStar Anti-ß$_2$GPI Domain 1**

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

Unmatched analytical performance*

- Highly sensitive and specific chemiluminescent immunoassays for superior accuracy and precision
- Extremely wide linearity ranges, with and without rerun
- 20 U/mL cut-off for all AcuStar Antiphospholipid Syndrome (APS) assays

Simple and efficient

- Cartridge-based, ready-to-use, precalibrated assays for unmatched simplicity
- Up to 60 day onboard stability—optimal for analysis 24/7
- Uses serum or citrated plasma samples
- Single set of controls for entire APS panel saves time and improves accuracy

*Compared to traditional ELISA methods.

HemosIL®

Complete solution for APS investigation

- FDA-cleared as an aid in the diagnosis of thrombotic disorders related to primary and secondary APS with other clinical findings
- Lupus Anticoagulant (LA) testing on ACL TOP Family systems combined with antiphospholipid (aPL) testing on ACL AcuStar systems provides a complete laboratory assessment for APS[1]



APS overview

APS, or Hughes Syndrome, is an autoimmune disorder

Definition and Incidence

- Caused by autoantibodies (aPL antibodies) against phospholipid-binding proteins (Cardiolipin, $ß_2$ Glycoprotein-I)
- Characterized by recurrent arterial and venous thrombosis, recurrent pregnancy loss and presence of circulating aPL antibodies
- Affects women five times more than men[1]

Classification

- Primary APS (PAPS)—presents with no known associated systemic disease or underlying condition
- Secondary APS (SAPS)—presents with underlying conditions, such as Systemic Lupus Erythematosus (SLE), other connective tissue disease, or medication

Clinical Events

- Venous and arterial thrombosis, most commonly in the deep venous system of the lower limb[2]
- Recurrent miscarriages and pregnancy complications, particularly late-pregnancy loss[3]

Diagnostic Criteria

APS diagnosis requires the presence of one clinical criterion and one laboratory criterion.[4]

Clinical Criteria	Laboratory Criteria
1. Vascular thrombosis (arterial, venous) **2. Pregnancy morbidity** • Unexplained fetal death beyond 10th week • Premature birth before 34th week • Three or more unexplained spontaneous abortions before 10th week	**1. LA antibodies** • Two occasions, at least 12 weeks apart **2. Anti-Cardiolipin (aCL) antibodies** • Medium or high titer of IgG and/or IgM • Two occasions, at least 12 weeks apart **3. Anti-$ß_2$ Glycoprotein-I (a$ß_2$GPI) antibodies** • IgG and/or IgM • Two occasions, at least 12 weeks apart

Non-Criteria Testing

- Additional non-criteria testing has shown to be beneficial in the diagnosis of APS
- $ß_2$ GPI IgG Domain 1 is the primary target for autoantibodies associated with APS
- Presence of Domain 1 antibodies is a strong indicator for clinical manifestations of APS[5]

Excellent analytical performance

HemosIL AcuStar APS assay panel characteristics

	aCL IgG	aCL IgM	aß$_2$ GPI IgG	aß$_2$ GPI IgM	aß$_2$ GPI D1
Linearity (U/mL)					
Without Rerun	2.6–2,024	1.0–774	6.4–6,100	1.1–841	3.6–1,380.4
With Rerun (up to)	40,480	15,480	122,000	16,820	3.6–13,804.0
Cut-off (U/mL)	20	20	20	20	20
Precision (aPL panel)	**Below Cut-off**				
Within Run (% CV)	< 8				< 10%
Total (% CV)	< 12				< 15%

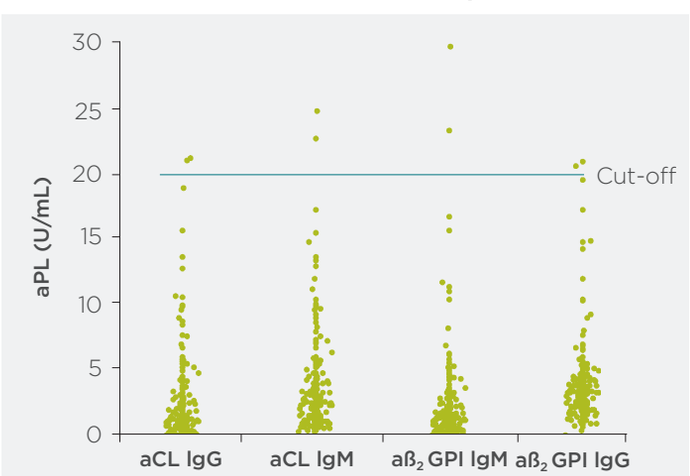
Assay standardization

A normal-range study of 252 citrated plasma samples from healthy donors was conducted.*[6]

Results

- Four HemosIL AcuStar APS assays were standardized to a cut-off of 20 U/mL, maximizing testing efficiency
- HemosIL AcuStar APS assays correlate with IgG chimeric antibody (HCAL) and IgM monoclonal antibody (EY2C9)

Standardization to Cut-off of 20 U/mL





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

Excellent clinical performance

Diagnostic agreement

A clinical study by de Moerloose *et al*[7] evaluated the diagnostic and predictive performance of the HemosIL AcuStar aPL panel (aCL IgG/IgM and aß$_2$ GPI IgG/IgM)

Methods

- 321 samples were blind-tested using the HemosIL AcuStar aPL* assay panel and three commercially available ELISAs

Patients and control group

- APS-confirmed patient samples included PAPS and SAPS
- Control group included:
  - Apparently healthy donors (normal)
  - SLE without APS
  - SLE-like
  - Other autoimmune cardiovascular disorders

Results

- HemosIL AcuStar aPL assays demonstrated:
  - Good balance of sensitivity and specificity vs ELISA
  - Excellent agreement with APS diagnosis

	HemosIL AcuStar aPL	ELISA 1	ELISA 2	ELISA 3
Sensitivity (%) CI (%)	**72.8** 62.6–81.6	**75.0** 64.9–83.4	**57.6** 46.9–67.9	**64.1** 53.5–73.9
Specificity (%) CI (%)	**87.3** 82.3–91.4	**74.2** 68.1–79.8	**85.6** 80.4–89.9	**88.6** 83.8–92.4
Agreement (%) CI (%)	**83.2** 78.6–87.1	**74.5** 69.3–79.1	**77.6** 72.6–82.0	**81.6** 76.9–85.7

*HemosIL AcuStar aPL assays were tested using a cut-off of 20 U/mL.

NEW

HemosIL AcuStar Anti-ß$_2$GPI Domain 1 assay

- Cut-off aligns with clinically validated APS criteria assays
- Ease-of-use and consistent interpretation
- Optimizes assay sensitivity and specificity

Methods

- 1,090 samples were tested using HemosIL AcuStar Anti-ß$_2$GPI Domain 1 and a commercially available aß$_2$ GPI IgG ELISA

Patients and control group

- APS-confirmed patient samples included PAPS and SAPS
- Control group included:
  - Infectious diseases
  - Various autoimmune disorders
  - Disorders suggestive of APS but excluded from APS diagnosis

Results

- HemosIL AcuStar Anti-ß$_2$GPI Domain 1 demonstrated:
  - Good sensitivity and superior specificity for APS
  - Excellent agreement with commercially available ELISA

Excellent agreement with clinical diagnosis (n=1,090)	Diagnosis			Agreement (95% CI)
	APS	Not APS	Total	
Positive	138	3	141	Sensitivity = 51.1% (45.0–57.2%)
Negative	132	817	949	Specificity = 99.6% (98.9–99.9%)

The simplicity and efficiency of chemiluminescence

Enhances efficiency and simplicity in specialty testing

No advanced training or extensive manual processes required

Fully automated chemiluminescent immunoassay technology

Minimizes optical interferences

Cartridge-based assays

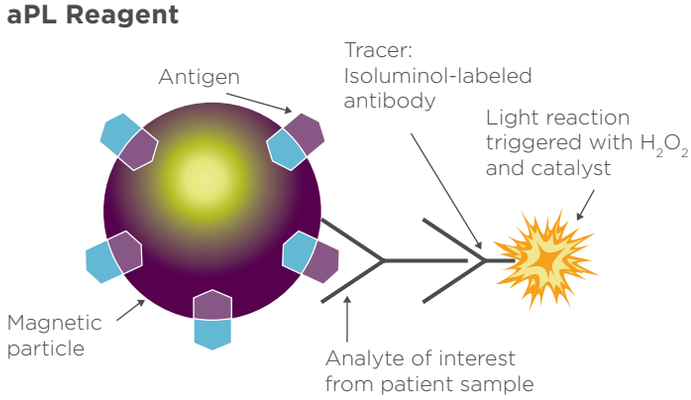
Facilitates test processing, QC and calibration

ACL AcuStar HEMOSTASIS TESTING SYSTEM

Principle

- Magnetic particles are coated with $ß_2$ GPI ($aß_2$ GPI antibody assays), cardiolipin and $ß_2$ GPI (aCL antibody assays), or recombinant $ß_2$ GPI Domain 1 ($aß_2$ GPI Domain 1 assay)
- Antigen-coated magnetic particles capture aPL antibodies if present in sample
- Next, an isoluminol-labeled secondary antibody in the tracer binds to the captured antibodies
- With the addition of triggers, light is emitted proportionate to the concentration of antibodies

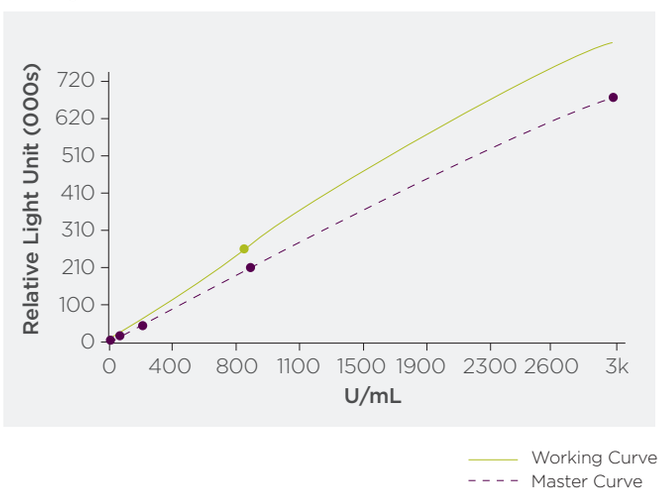
aPL Reagent



Calibration

- Easy assay setup with reagent cartridge barcode that automatically imports:
  - Assay type
  - Predefined, lot-specific master calibration curve
- Calibration adjusted only once per cartridge lot change
- Uses two calibration levels, included in kit, to adjust master curve

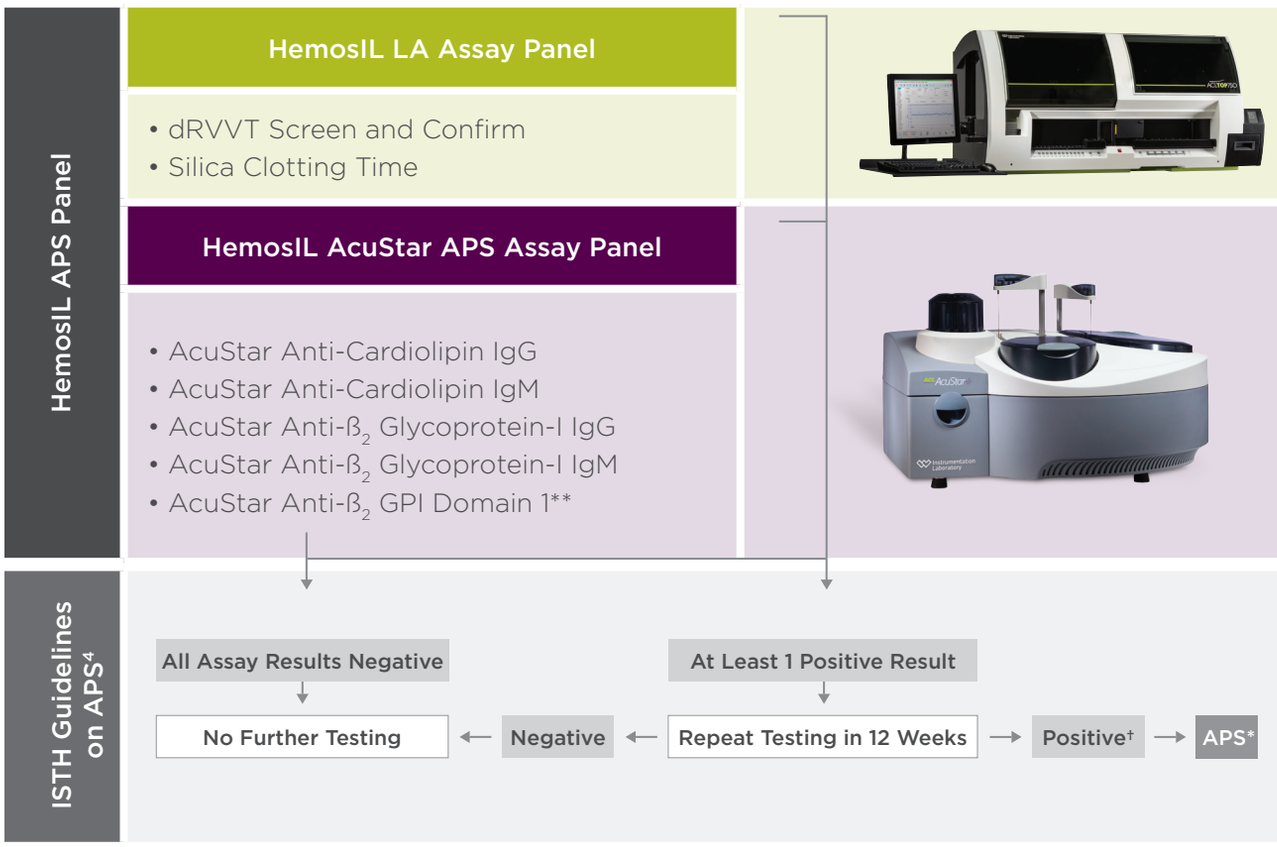
Assay Calibration on the ACL AcuStar



A complete solution for APS investigation

A complete APS diagnostic assessment

LA testing on the ACL TOP together with aPL testing on ACL AcuStar meets ISTH laboratory guidelines[1,6] for a complete APS diagnosis.[8]

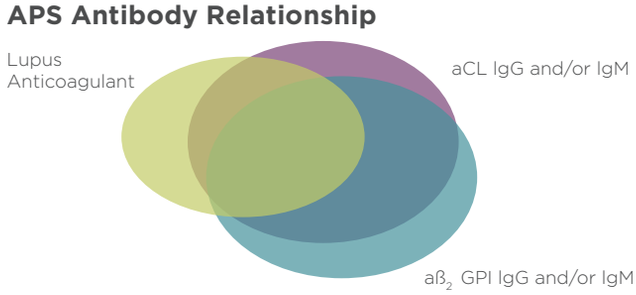


*Both clinical and laboratory criteria must be met in order to diagnose APS. Refer to ISTH Guidelines on APS Diagnosis 2006.
**Not currently included in APS classification criteria.
†The same assay must be repeatedly positive.

Maximum efficiency in APS detection

- APS patients may have positive results for one or more aPL antibodies, including LA, aCL IgG and/or IgM and aß$_2$ GPI IgG and/or IgM
- Therefore, using the entire assay panel optimizes laboratory investigation of APS

APS Antibody Relationship



HemosIL AcuStar Multi-Ab Controls offer enhanced efficiency

- Single kit of liquid, ready-to-use, multi-assay controls for AcuStar aPL and HIT assays
- Fully automated on the ACL AcuStar
- Time savings for increased lab efficiency
- Improved accuracy for better patient care

HemosIL AcuStar Antiphospholipid Assay Panel

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-$ß_2$ Glycoprotein-I IgG	0009802012	1 Cartridge (50 tests) Anti-$ß_2$ Glycoprotein-I IgG Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
HemosIL AcuStar Anti-$ß_2$ Glycoprotein-I IgM	0009802016	1 Cartridge (50 tests) Anti-$ß_2$ Glycoprotein-I IgM Calibrator 1, 1 x 1 mL (liq) Calibrator 2, 1 x 1 mL (liq)
NEW HemosIL AcuStar Anti-$ß_2$GPI Domain 1	00009800015	1 Cartridge (50 tests) Anti-$ß_2$GPI Domain 1 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-$ß_2$ Glycoprotein-I IgG Controls	0009802112	Low Anti-$ß_2$ GPI IgG Control, 3 x 1 mL (liq) High Anti-$ß_2$ GPI IgG Control, 3 x 1 mL (liq)
HemosIL AcuStar Anti-$ß_2$ Glycoprotein-I IgM Controls	0009802116	Low Anti-$ß_2$ GPI IgM Control, 3 x 1 mL (liq) High Anti-$ß_2$ GPI IgM Control, 3 x 1 mL (liq)
HemosIL AcuStar Multi-Ab Controls	00009800003	Low Multi-Ab Control, 3 x 2 mL (liq) High Multi-Ab Control, 3 x 2 mL (liq)
NEW HemosIL AcuStar Anti-$ß_2$GPI Domain 1 Controls	00009800022	Low Anti-$ß_2$ GPI D1 Control 3 x 1 mL (liq) High Anti-$ß_2$ GPI D1 Control 3 x 1 mL (liq)

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