

# THROMBOSIS PRODUCT HIGHLIGHTS

AESKU.DIAGNOSTICS has extensive experience and know-how in the Anti-Phospholipid Syndrome (APS) field and offers the most comprehensive panel of anti-phospholipid tests, employing highly purified, native human  $\beta$ 2-GP-1 antigens and bovine phospholipids, available in different kit formats and immunoglobulins.

Two major serological parameters for diagnosis, anti-cardiolipin and anti- $\beta$ 2-GP-1 antibodies are well established. Despite some contradictory results, a number of studies indicate that there is a sub-group of APS patients with a clear clinical picture of APS but without detectable Cardiolipin /  $\beta$ 2-GP-1 antibodies or LA.

There is, however, increasing evidence from a number of studies that testing a profile of various phospholipids, rather than restriction to cardiolipin and  $\beta$ 2-GP-1, increases both the sensitivity and specificity of the laboratory diagnosis.

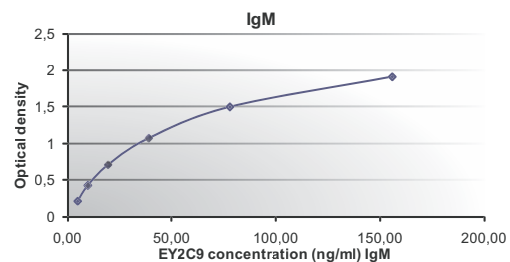
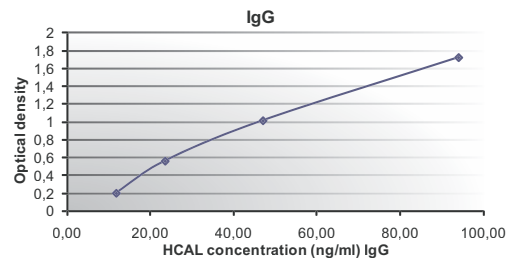
## Why choose AESKULISA® Cardiolipin and $\beta$ 2-GP-1 tests?

- Kit format flexibility: **AESKULISA® ACA** and  **$\beta$ 2-GP-1** kits allow the separated as well as combined detection of ACA and  $\beta$ 2-GP-1 antibodies of the IgG, IgM and IgA isotype.

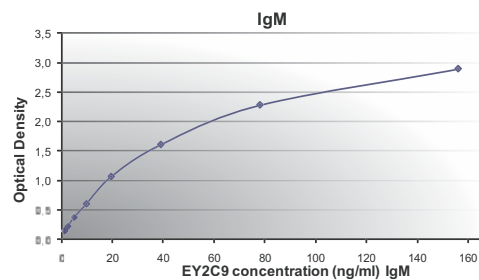
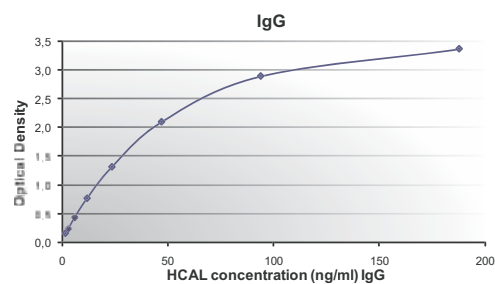
- Kit conjugate flexibility: Combined detection of all isotypes can be performed with the ACA-Check and  $\beta$ 2-GP-1 Check.

The ACA and  $\beta$ 2-GP-1 GM kit format include the individual IgG and IgM conjugates within the same kit for a cost effective and convenient handling.

- Usage of native human  $\beta$ 2 -GP-1 instead of bovine.
- Addition of  $\beta$ 2-GP-1 during coating.
- Coating with a defined and reproducible ratio of cardiolipin to  $\beta$ 2-GP-1 is ensured.
- Dedicated phospholipids' dilution and wash buffers are not necessary: THE "ONE" AESKU CONCEPT.
- Calibration of Cardiolipin IgG, IgM and IgA against the Harris sera (GPL and MPL units).
- Calibration of Cardiolipin IgG against the UK NEQAS standard preparation 97/514.
- Standardization of Cardiolipin-GM and  $\beta$ 2-GP-1-GM using the Sapporo monoclonal antibodies (Sapporo standards). Reporting units can be converted to ng/ml.



Testing of monoclonal antibodies HCAL and EY2C9 (Sapporo-Standards) on **AESKULISA®** Cardiolipin-GM Test



Testing of monoclonal antibodies HCAL and EY2C9 (Sapporo-Standards) on **AESKULISA®**  $\beta$ 2-GP-1-GM tests

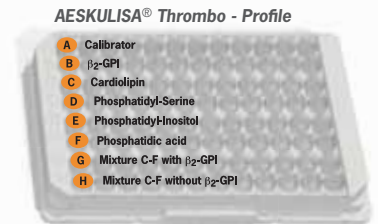
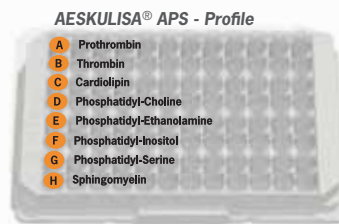
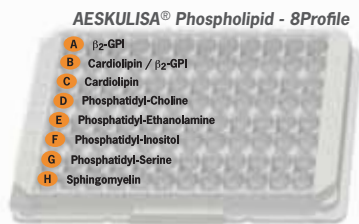
# THROMBOSIS PRODUCT HIGHLIGHTS

**AESKULISA®** Phospholipid screening tests are highly sensitive for a rapid and reliable combined determination of the most important antiphospholipid antibodies.

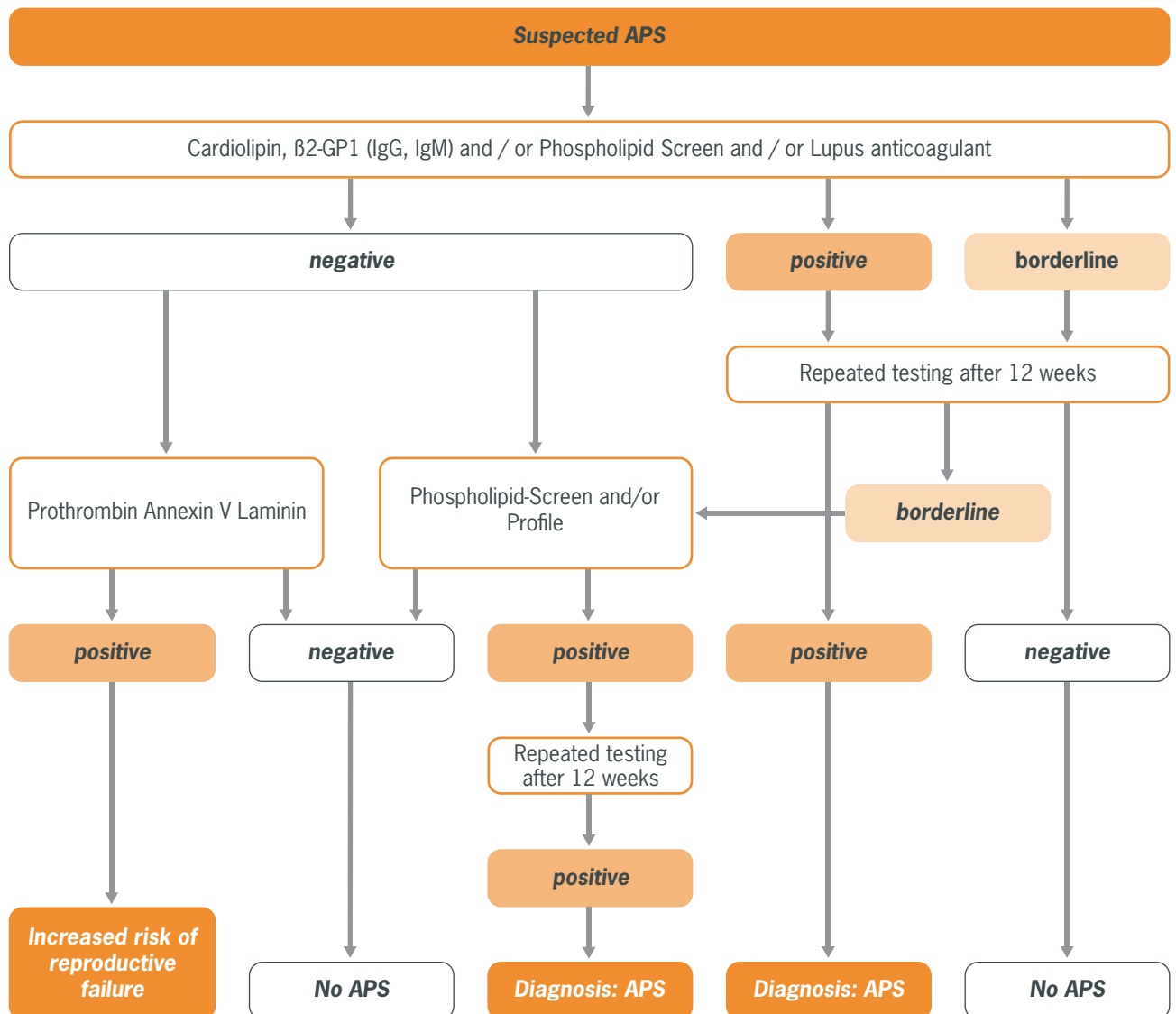
**AESKULISA®** Phospholipid profiles, employing eight different antigens, are the ideal tools for the reliable differential diagnosis of APS, as certain antibody patterns can be correlated with distinct clinical manifestations of the APS.

Antibody against	Sensitivity (%)	Specificity (%)
Cardiolipin	67	73
$\beta_2$ -Glycoprotein I	69	69
Phosphatidylserine	62	83
Phosphatidylinositol	69	75
P-Ethanolamine	62	78
Phosphatidylcholine	62	79

All phospholipids are also available as single tests for a cost-effective therapy monitoring.



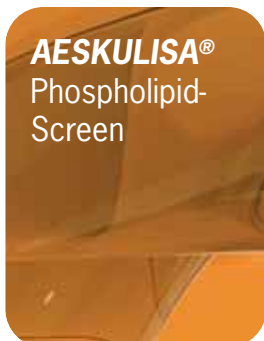
## Proposed diagnostic workflow for APS



A definite clinical diagnosis should not be based on the results of the performed tests alone, but should be made by the physician after all clinical and laboratory findings have been evaluated. The diagnosis is to be verified using different diagnostic methods.

# THROMBOSIS

REF 3216



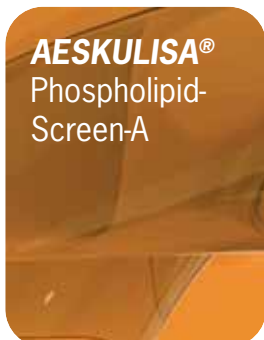
**AESKULISA®**  
Phospholipid-Screen

**Conjugate:**  
anti-human IgG/M-HRP  
**Cut-off:**  
Cut-off calibrator  
**Kit Configuration:**  
Screening-Check

**Antigens coated:**  
Each well with native human  $\beta$ 2-glycoprotein I and cardiolipin, phosphatidyl-choline, -ethanolamine, -inositol, -serine and sphingomyelin

Enzyme-linked immunoassay (ELISA) for the combined qualitative determination of IgG and IgM autoantibodies to phospholipids (SCREENING) in human serum

REF 3219



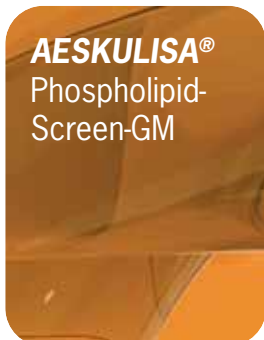
**AESKULISA®**  
Phospholipid-Screen-A

**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Screening-A

**Antigens coated:**  
Each well with native human  $\beta$ 2-glycoprotein I and cardiolipin, phosphatidyl-choline, -ethanolamine, -inositol, -serine and sphingomyelin

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to phospholipids (SCREENING) in human serum

REF 3224



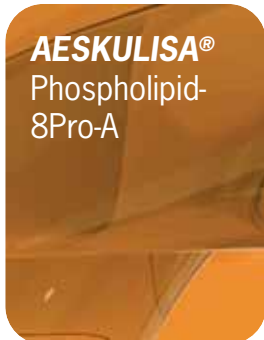
**AESKULISA®**  
Phospholipid-Screen-GM

**Conjugate:**  
anti-human IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Screening-GM

**Antigens coated:**  
Each well with native human  $\beta$ 2-glycoprotein I and cardiolipin, phosphatidyl-choline, -ethanolamine, -inositol, -serine and sphingomyelin

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phospholipids (SCREENING) in human serum

REF 3222



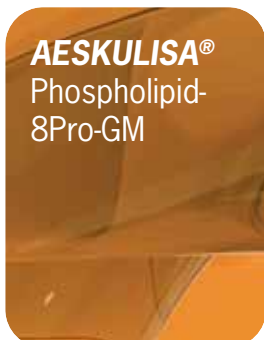
**AESKULISA®**  
Phospholipid-8Pro-A

**Conjugate:**  
anti-human IgA-HRP  
**Cut-off Calibrator:**  
antigen specific  
**Kit Configuration:**  
Profile-A

**Antigens coated:**  
 $\beta$ 2-glycoprotein I, cardiolipin+  $\beta$ 2-glycoprotein I, cardiolipin, phosphatidyl-choline, -ethanolamine, -inositol, -serine and sphingomyelin

Enzyme-linked immunoassay (ELISA) for the qualitative determination of 8 different IgA anti-phospholipid autoantibodies (PROFILE) in human serum

REF 3232



**AESKULISA®**  
Phospholipid-8Pro-GM

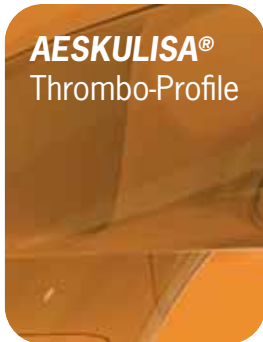
**Conjugate:**  
anti-human IgG-HRP + IgM-HRP  
**Cut-off Calibrator:**  
antigen specific  
**Kit Configuration:**  
Profile-GM

**Antigens coated:**  
 $\beta$ 2-glycoprotein I, cardiolipin +  $\beta$ 2-glycoprotein I, cardiolipin, phosphatidyl-choline, -ethanolamine, -inositol, -serine and sphingomyelin

Enzyme-linked immunoassay (ELISA) for the separate qualitative determination of 8 different IgG and/or IgM anti-phospholipid autoantibodies (PROFILE) in human serum

# THROMBOSIS

REF 3230



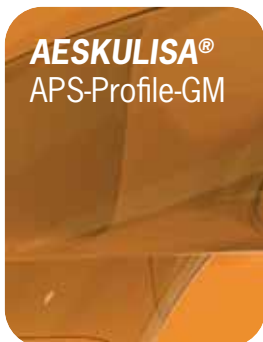
**AESKULISA®**  
Thrombo-Profile

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Profile-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
and cardiolipin, phosphatidyl-  
serine, -inositol and phosphatidic  
acid as well as mixtures  
thereof

Enzyme-linked immunoassay  
(ELISA) for the separate quantitative  
and qualitative determination of  
IgG and/or IgM autoantibodies in  
human serum to  $\beta$ 2-glycoprotein I,  
cardiolipin, phosphatidyl-serine,  
-inositol, phosphatidic acid, a mixture  
of all phospholipids and a mixture  
of all phospholipids without additional  
 $\beta$ 2-glycoprotein I coating

REF 3234



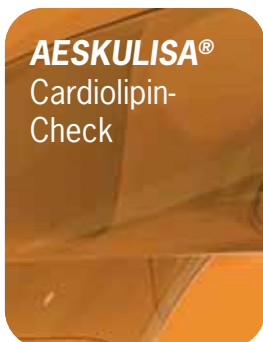
**AESKULISA®**  
APS-Profile-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Cut-off Calibrator:**  
antigen specific  
**Kit Configuration:**  
Profile-GM

**Antigens coated:**  
Human prothrombin, thrombin,  
cardiolipin, phosphatidyl-choline-  
ethanolamine, -inositol, -serine  
and sphingomyelin

Enzyme-linked immunoassay  
(ELISA) for the separate qualitative  
determination of 8 different  
IgG and/or IgM antiphospholipid  
autoantibodies (PROFILE) in  
human serum

REF 3202



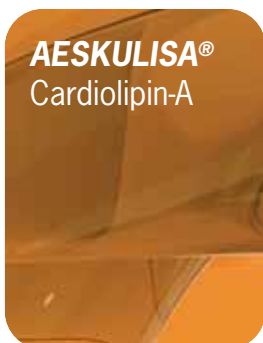
**AESKULISA®**  
Cardiolipin-  
Check

**Conjugate:**  
anti-human  
IgA/G/M-HRP  
**Equivocal Zone:**  
16 - 24 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-Check

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ cardiolipin

Enzyme-linked immunoassay  
(ELISA) for the combined quantitative  
and qualitative determination of  
IgA, IgG and IgM autoantibodies  
to the cardiolipin- $\beta$ 2-glycoprotein  
I complex in human serum

REF 3203



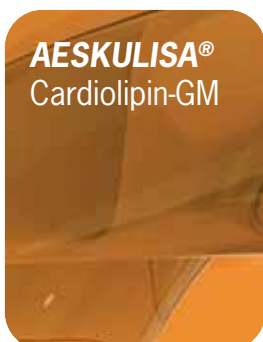
**AESKULISA®**  
Cardiolipin-A

**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 APL/ml  
**Standard Range:**  
0 - 300 APL/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ cardiolipin

Enzyme-linked immunoassay  
(ELISA) for the quantitative and  
qualitative determination of IgA  
autoantibodies to the cardiolipin- $\beta$ 2-  
glycoprotein I complex

REF 3204



**AESKULISA®**  
Cardiolipin-GM

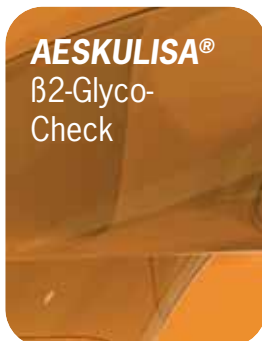
**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 GPL/M-  
PL/ml  
**Standard Range:**  
0 - 300 GPL/MPL/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ cardiolipin

Enzyme-linked immunoassay  
(ELISA) for the separate quantitative  
and qualitative determination of  
IgG and/or IgM autoantibodies  
to the cardiolipin- $\beta$ 2-glycoprotein  
I complex in human serum

# THROMBOSIS

REF 3215



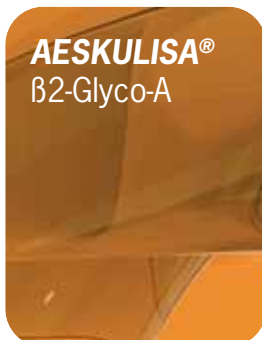
**AESKULISA®**  
B2-Glyco-  
Check

**Conjugate:**  
anti-human  
IgA/G/M-HRP  
**Equivocal Zone:**  
16 - 24 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-Check

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgA, IgG and IgM autoantibodies to  $\beta$ 2-glycoprotein I in human serum

REF 3205



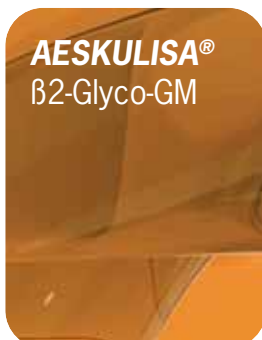
**AESKULISA®**  
B2-Glyco-A

**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to  $\beta$ 2-glycoprotein I in human serum

REF 3206



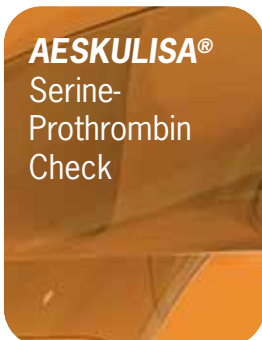
**AESKULISA®**  
B2-Glyco-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to  $\beta$ 2-glycoprotein I in human serum

REF 3223



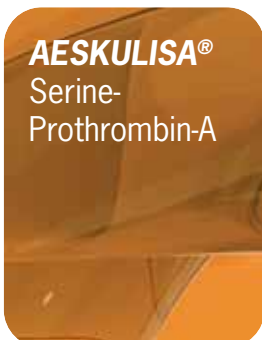
**AESKULISA®**  
Serine-  
Prothrombin  
Check

**Conjugate:**  
anti-human  
IgG/M-HRP  
**Equivocal Zone:**  
16 - 24 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-Check

**Antigens coated:**  
Native human prothrombin-phosphatidylserine complex

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgG and IgM autoantibodies to the prothrombin-phosphatidylserine-complex in human serum

REF 3227



**AESKULISA®**  
Serine-  
Prothrombin-A

**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human prothrombin-phosphatidylserine complex

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to the prothrombin-phosphatidylserine-complex in human serum

# THROMBOSIS

REF 3226

**AESKULISA®**  
Serine-  
Prothrombin-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human prothrombin-phosphatidylserine complex

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to the prothrombin-phosphatidylserine-complex in human serum

REF 3211

**AESKULISA®**  
Prothrombin-  
Check

**Conjugate:**  
anti-human  
IgG/M-HRP  
**Equivocal Zone:**  
16 - 24 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-Check

**Antigens coated:**  
Native human prothrombin

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgG and IgM autoantibodies to prothrombin in human serum

REF 3210

**AESKULISA®**  
Prothrombin-A

**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human prothrombin

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to prothrombin in human serum

REF 3229

**AESKULISA®**  
Prothrombin-  
GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human prothrombin

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to prothrombin in human serum

REF 3244

**AESKULISA®**  
Cardiolipin-GM

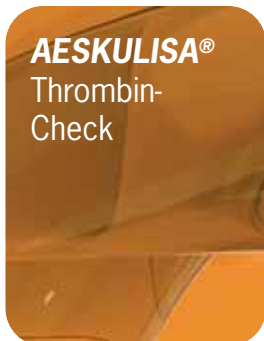
**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 GPL/MPL/ml  
**Standard Range:**  
0 - 140 GPL/MPL/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I + cardiolipin

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to the cardiolipin- $\beta$ 2-glycoprotein I complex in human serum

# THROMBOSIS

REF 3225



**AESKULISA®**  
Thrombin-  
Check

**Conjugate:**  
anti-human  
IgA/G/M-HRP

**Equivocal Zone:**  
16 - 24 U/ml

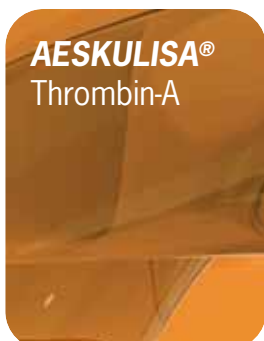
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-Check

**Antigens coated:**  
Native human thrombin

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgA, IgG and IgM autoantibodies to thrombin in human serum

REF 3213



**AESKULISA®**  
Thrombin-A

**Conjugate:**  
anti-human IgA-HRP

**Equivocal Zone:**  
12 - 18 U/ml

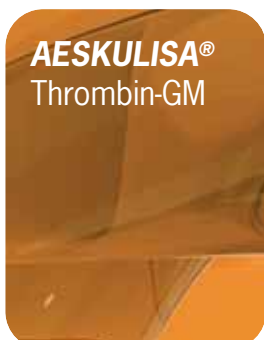
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human thrombin

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to thrombin in human serum

REF 3228



**AESKULISA®**  
Thrombin-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

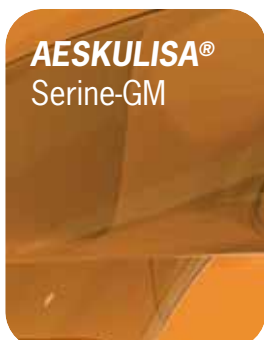
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human thrombin

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to thrombin in human serum

REF 3207



**AESKULISA®**  
Serine-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

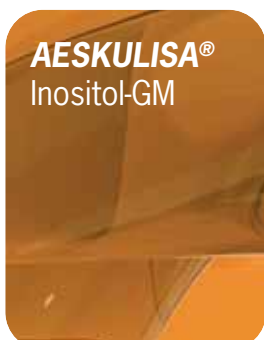
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylserine

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidylserine in human serum

REF 3208



**AESKULISA®**  
Inositol-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylinositol

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidylinositol in human serum

# THROMBOSIS

REF 3236

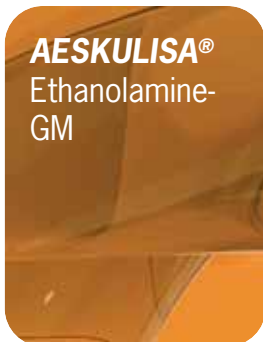


**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylethanolamine

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to phosphatidylethanolamine in human serum

REF 3209

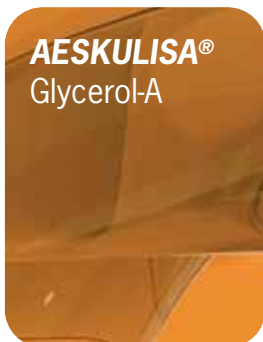


**Conjugate:**  
anti-human IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylethanolamine

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidylethanolamine in human serum

REF 3254

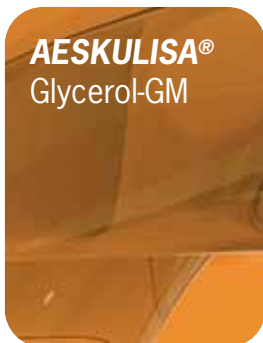


**Conjugate:**  
anti-human IgA-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-A

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylglycerol

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgA autoantibodies to phosphatidylglycerol in human serum

REF 3255

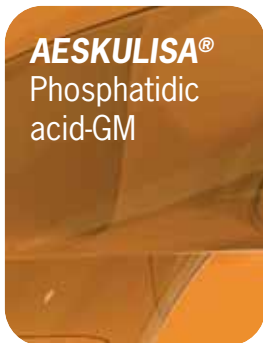


**Conjugate:**  
anti-human IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylglycerol

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidylglycerol in human serum

REF 3231



**Conjugate:**  
anti-human IgG-HRP + IgM-HRP  
**Equivocal Zone:**  
12 - 18 U/ml  
**Standard Range:**  
0 - 300 U/ml  
**Kit Configuration:**  
Single-GM

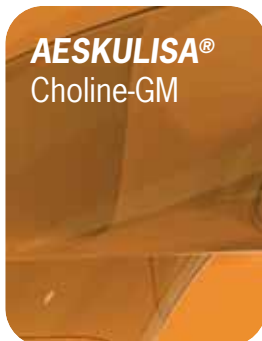
**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidic acid

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidic acid in human serum



# THROMBOSIS

REF 3212



**AESKULISA®**  
Choline-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

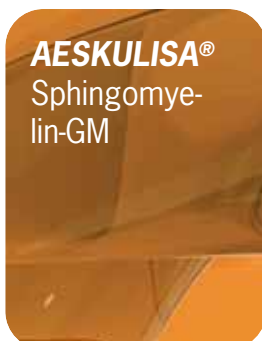
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ phosphatidylcholine

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to phosphatidylcholine in human serum

REF 3214



**AESKULISA®**  
Sphingomyelin-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

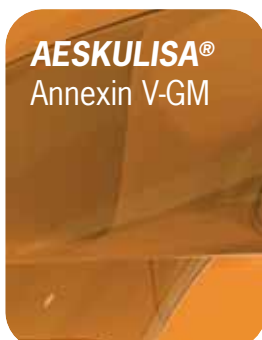
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human  $\beta$ 2-glycoprotein I  
+ sphingomyelin

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to sphingomyelin in human serum

REF 3240



**AESKULISA®**  
Annexin V-GM

**Conjugate:**  
anti-human  
IgG-HRP + IgM-HRP

**Equivocal Zone:**  
12 - 18 U/ml

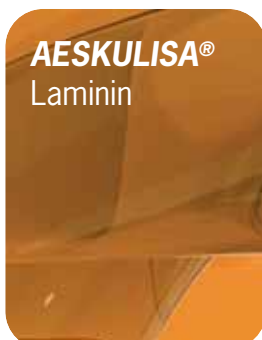
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-GM

**Antigens coated:**  
Native human annexin V

Enzyme-linked immunoassay (ELISA) for the separate quantitative and qualitative determination of IgG and/or IgM autoantibodies to annexin V in human serum

REF 3235



**AESKULISA®**  
Laminin

**Conjugate:**  
anti-human IgG-HRP

**Equivocal Zone:**  
12 - 18 U/ml

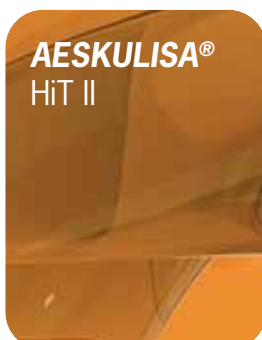
**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-G

**Antigens coated:**  
Native human laminin-1

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgG autoantibodies against laminin-1 in human serum

REF 3290



**AESKULISA®**  
HiT II

**Conjugate:**  
anti-human IgG-HRP

**Equivocal Zone:**  
12 - 18 U/ml

**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-G

**Antigens coated:**  
HiT II complex

Enzyme-linked immunoassay (ELISA) for the quantitative and qualitative determination of IgG autoantibodies that cause heparin induced thrombocytopenia type II in human serum

REF 3291

**AESKULISA®**  
HiT II Check

**Conjugate:**  
anti-human  
Ig A/G/M-HRP

**Equivocal Zone:**  
16 - 24 U/ml

**Standard Range:**  
0 - 300 U/ml

**Kit Configuration:**  
Single-Check

**Antigens coated:**  
HiT II complex

Enzyme-linked immunoassay (ELISA) for the combined quantitative and qualitative determination of IgA, IgG and IgM autoantibodies that cause heparin induced thrombocytopenia type II in human serum