ORGENTEC

EG Konformitätserklärung

EC Declaration of Conformity

ORGENTEC Diagnostika GmbH
Carl-Zeiss-Straße 49-51, 55129 Mainz, GERMANY

Wir erklären in eigener Verantwortung, dass das ORGENTEC Produkt

We declare in our sole responsibility that the ORGENTEC product

ORG 510 Anti-Sm

zur quantitativen in-vitro-Bestimmung bestimmt ist und entsprechend Art. 9 Abs. Satz 1 der Europäischen Richtlinie 98/79/EG als „Sonstige Produkte" (non-A, non-B, keine Selbstanwendung) klassifiziert ist.

as intended for use in quantitative in vitro determination is classified as "Other Devices" (non-A, non-B, no self-testing device) *according to article 9 paragraph 1 sentence 1 of the European directive 98/79/EC.*

Das Produkt stimmt mit den Grundlegenden Anforderungen und allen zutreffenden Bestimmungen der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998 über in-vitro-Diagnostika überein. Die Konformität zur Richtlinie wurde durch ein Konformitätsbewertungsverfahren nach Anhang III der Richtlinie festgestellt.

This product is conform with the essential requirements and meet the appropriate provisions of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. Conformity was proved by a conformity assessment procedure referred to in annex III of the directive.

Liste angewendeter Normen:

List of standards applied for CE marking:
EN ISO 13485, EN ISO 14971, EN ISO 18113, EN ISO 15223, EN ISO 23640, EN 13612.

Mainz, 2021-02-05

René Betz
Head of Regulatory Affairs

ORGENTEC Diagnostika GmbH
ORGENTEC
CE and ISO-certified
Carl-Zeiss-Str. 49-51, 55129 Mainz, GERMANY

Gültig ab / Valid from 2021-02-05 bis / until 2024-02-28

Notification pursuant to §25 Abs. 3 Nr. 3 Medical Devices Act, MPG
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EDMS 12-10-01-11-00
GMDN 55148

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510_3

ORG 510 Anti-Sm

INTENDED PURPOSE

Anti-Sm is an ELISA test system for the quantitative measurement of IgG class autoantibodies against Sm in human serum or plasma. This product is intended for professional in vitro diagnostic use only.

The detection of autoantibodies against Sm proteins is a component of the multi-parametric ACR criteria for the diagnosis of systemic lupus erythematosus (SLE). The detection of Sm antibodies serves as a prognostic marker for SLE, there is a relationship between the appearance of Sm antibodies and severe organ manifestations of the disease. Evaluation of a test result should always take into account all clinical and laboratory diagnostic findings.

SYMBOLS USED ON LABELS

IVD	In vitro diagnostic medical device
	Manufacturer
REF	Catalogue number
Σ 96	Sufficient for 96 determinations
LOT	Batch code
	Use by
2°C 8°C	Temperature limitation
	Keep away from sunlight
	Do not reuse
	Date of manufacture
CE	CE marked according to 98/79/EC
	Consult instructions for use
510_3	Electronic Instruction For Use: version

MICROPLATE	Microplate
CALIBRATOR A	Calibrator
CALIBRATOR B	Calibrator
CALIBRATOR C	Calibrator
CALIBRATOR D	Calibrator
CALIBRATOR E	Calibrator
CALIBRATOR F	Calibrator
CONTROL +	Control positive
CONTROL −	Control negative
DILUENT	Sample Buffer P
CONJUGATE	Enzyme Conjugate
TMB	TMB Substrate
STOP	Stop solution
WASH	Wash Buffer
RTU	Ready to use

PRINCIPLE OF THE TEST

Highly purified Sm is bound to microwells.
The determination is based on an indirect enzyme linked immune reaction with the following steps:
Specific antibodies in the patient sample bind to the antigen coated on the surface of the reaction wells. After incubation, a washing step removes unbound and unspecifically bound serum or plasma components. Subesquently added enzyme conjugate binds to the immobilized antibody-antigen-complexes. After incubation, a second washing step removes unbound enzyme conjugate. After addition of substrate solution the bound enzyme conjugate hydrolyses the substrate forming a blue coloured product. Addition of an acid stopps the reaction generating a yellow end-product. The intensity of the yellow color
correlates with the concentration of the antibody-antigen-complex and can be measured photometrically at 450 nm.

WARNINGS AND PRECAUTIONS

- All reagents of this kit are intended for professional in vitro diagnostic use only.
- Components containing human serum were tested and found negative for HBsAg, HCV, HIV1 and HIV2 by FDA approved methods. No test can guarantee the absence of HBsAg, HCV, HIV1 or HIV2, and so all human serum based reagents in this kit must be handled as though capable of transmitting infection.
- Bovine serum albumin (BSA) used in components has been tested for BSE and found negative.
- Avoid contact with the substrate TMB (3,3´,5,5´-Tetramethyl-benzidine).
- Stop solution contains acid, classifiaction is non-hazardous. Avoid contact with skin.
- Control, sample buffer and wash buffer contain sodium azide 0.09% as preservative. This concentration is classified as non-hazardous.
- Enzyme conjugate contains ProClin 300 0.05% as preservative. This concentration is classified as non-hazardous.

During handling of all reagents, controls and serum samples observe the existing regulations for laboratory safety regulations and good laboratory practice:

- First aid measures: In case of skin contact, immediately wash thoroughly with water and soap. Remove contaminated clothing and shoes and wash before reuse. If system fluid comes into contact with skin, wash thoroughly with water. After contact with the eyes carefully rinse the opened eye with running water for at least 10 minutes. Get medical attention if necessary.
- Personal precautions, protective equipment and emergency procedures:

Observe laboratory safety regulations. Avoid contact with skin and eyes. Do not swallow. Do not pipette by mouth. Do not eat, drink, smoke or apply makeup in areas where specimens or kit reagents are handled. When spilled, absorb with an inert material and put the spilled material in an appropriate waste disposal.

- Exposure controls / personal protection: Wear protective gloves of nitril rubber or natural latex. Wear protective glasses. Used according to intended use no dangerous reactions known.
- Conditions to avoid: Since substrate solution is light-sensitive. Store in the dark.
- For disposal of laboratory waste the national or regional legislation has to be observed.

Observe the guidelines for performing quality control in medical laboratories by assaying control sera.

CONTENTS OF THE KIT

ORG 510	Σ 96	Sufficient for 96 determinations
MICROPLATE	1	One divisible microplate consisting of 12 modules of 8 wells each. Ready to use. Color code on module
CALIBRATOR A	1x 1.5 ml	Calibrator A 0 U/ml, containing serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR B	1x 1.5 ml	Calibrator B 12.5 U/ml, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR C	1x 1.5 ml	Calibrator C 25 U/ml, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR D	1x 1.5 ml	Calibrator D 50 U/ml, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR E	1x 1.5 ml	Calibrator E 100 U/ml, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR F	1x 1.5 ml	Calibrator F 200 U/ml, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CONTROL +	1x 1.5 ml	Control positive, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
CONTROL −	1x 1.5 ml	Control negative, containing Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
DILUENT	20 ml	Sample Buffer P, containing PBS, BSA, detergent, preservative sodium azide 0.09%, yellow, concentrate (5 x).
CONJUGATE	15 ml	Enzyme Conjugate containing anti-human IgG antibodies, HRP labelled; PBS, BSA, detergent, preservative PROCLIN 0.05%, light red. Ready to use.
TMB	15 ml	TMB Substrate; containing 3,3', 5,5'- Tetramethylbenzidin, colorless. Ready to use.
STOP	15 ml	Stop solution; contains acid. Ready to use.
WASH	20 ml	Wash Buffer, containing Tris, detergent, preservative sodium azide 0.09%; 50 x conc.
	1	Certificate of Analysis

MATERIALS REQUIRED

- Microplate reader capable of endpoint measurements at 450 nm; optional: reference filter at 620 nm
- Data reduction software
- Multi-channel dispenser or repeatable pipette for 100 µl
- Vortex mixer
- Pipettes for 10 µl, 100 µl and 1000 µl
- Laboratory timing device
- Distilled or deionised water
- Measuring cylinder for 1000 ml and 100 ml
- Plastic container for storage of the wash solution

This ELISA assay is suitable for use on open automated ELISA processors. Each assay has to be validated on the respective automated system. Detailed information is provided upon request.

SPECIMEN COLLECTION, STORAGE AND HANDLING

- Collect whole blood specimens using acceptable medical techniques to avoid hemolysis.
- Allow blood to clot and separate the serum or plasma by centrifugation.
- Test serum should be clear and non-hemolyzed. Contamination by hemolysis or lipemia should be avoided, but does not interfere with this assay.
- Specimens may be refrigerated at 2-8°C for up to five days or stored at -20°C up to six months.
- Avoid repetitive freezing and thawing of serum or plasma samples. This may result in variable loss of antibody activity.
- Testing of heat-inactivated sera is not recommended.

STORAGE AND STABILITY

- Store test kit at 2-8°C in the dark.
- Do not expose reagents to heat, sun, or strong light during storage and usage.
- Store microplate sealed and dessicated in the clip bag provided.
- Shelf life of the unopended test kit is 18 months from day of production. Unopened reagents are stable until expiration of the kit. See labels for individual batch.
- Diluted Wash Buffer and Sample Buffer are stable for at least 30 days when stored at 2-8°C. We recommend consumption on the same day.

PROCEDURAL NOTES

- Do not use kit components beyond their expiration dates.
- Do not interchange kit components from different lots and products.
- All materials must be at room temperature (20-28°C) prior to use.
- Prepare all reagents and samples. Once started, performe the test without interruption.
- Double determinations may be done. By this means pipetting errors may become obvious.
- Perform the assay steps only in the order indicated.
- Always use fresh sample dilutions.
- Pipette all reagents and samples into the bottom of the wells.
- To avoid carryover or contamination, change the pipette tip between samples and different kit controls.
- Wash microwells thoroughly and remove the last droplets of wash buffer.
- All incubation steps must be accurately timed.
- Do not re-use microplate wells.

PREPARATION OF REAGENTS

WASH

Dilute the contents of one vial of the buffered wash solution concentrate (50x) with distilled or deionised water to a final volume of 1000 ml prior to use.

DILUENT

Sample Buffer P: Prior to use dilute the contents (20 ml) of one vial of sample buffer 5x concentrate with distilled or deionised water to a final volume of 100 ml.

Preparation of samples

Dilute patient samples 1:100 before the assay: Put 990 µl of prediluted sample buffer in a polystyrene tube and add 10 µl of sample. Mix well. Note: Calibrators / Controls are ready to use and need not be diluted.

TEST PROCEDURE

Prepare enough microplate modules for all calibrators / controls and patient samples.

1. Pipette **100 µl** of calibrators, controls and prediluted patient samples into the wells.
   Incubate for **30 minutes** at room temperature (20-28 °C).
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
2. Dispense **100 µ**l of enzyme conjugate into each well.
   Incubate for **15 minutes** at room temperature.
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
3. Dispense **100 µ**l of TMB substrate solution into each well.
   Incubate for **15 minutes** at room temperature
4. **Add 100 µl** of stop solution to each well of the modules
   Incubate for **5 minutes** at room temperature.
   Read the optical density at 450 nm (reference 600-690nm) and calculate the results.
   The developed colour is stable for at least 30 minutes. Read during this time.

Example for a pipetting scheme:

	1	2	3	4	5	6	7	8	9	10	11	12
A	A	P1										
B	B	P2										
C	C	P3										
D	D											
E	E											
F	F											
G	C+											
H	C-											

P1, ... patient sample A-F calibrators C+, C- controls

VALIDATION

Test results are valid if the optical densities at 450 nm for calibrators / controls and the results for controls comply with the reference ranges indicated on the Certificate of Analysis enclosed in each test kit.
If these quality control criteria are not met the assay run is invalid and should be repeated.

CALCULATION OF RESULTS

For quantitative results plot the optical density of each calibrator versus the calibrator concentration to create a calibration curve. The concentration of patient samples may then be estimated from the calibration curve by interpolation.
Using data reduction software a 4-Parameter-Fit with lin-log coordinates for optical density and concentration is the data reduction method of choice.

PERFORMANCE CHARACTERISTICS

Calibration

The assay system is calibrated against the internationally recognized reference sera from CDC, Atlanta USA.

Measuring range

The calculation range of this ELISA assay is 0 - 200 U/ml

Expected values

In a normal range study with samples from healthy blood donors the following ranges have been established with this ELISA assay: Cut-off 25 U/ml

Interpretation of results

Negative:	< 15 U/ml
Borderline:	15 - 25 U/ml
Positive:	> 25 U/ml

Linearity

Patient samples containing high levels of specific antibody were serially diluted in sample buffer to demonstrate the dynamic range of the assay and the upper / lower end of linearity. Activity for each dilution was calculated from the calibration curve using a 4-Parameter-Fit with lin-log coordinates.

Sample	Dilution	Observed U/ml	Expected U/ml	O/E [%]
1	1:100	161.4	161.4	100
	1:200	81.0	80.7	100
	1:400	39.1	40.4	97
	1:800	19.3	20.2	96
2	1:100	292.6	292.6	100
	1:200	146.9	146.3	100
	1:400	73.3	73.2	100
	1:800	35.3	36.6	97

Limit of detection

Functional sensitivity was determined to be: 1 U/ml

Reproducibility

Intra-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 24 determinations in a single run. Results for precision-within-assay are shown in the table below.
Inter-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 6 determinations in 5 different runs. Results for run-to-run precision are shown in the table below.

Intra-Assay		
Sample	Mean U/ml	CV %
1	51.4	4.1
2	84.8	2.0
3	157.2	2.6

Inter-Assay		
Sample	Mean U/ml	CV %
1	53.3	5.3
2	83.7	2.6
3	153.9	1.3

Interfering substances

No interference has been observed with haemolytic (up to 1000 mg/dl) or lipemic (up to 3 g/dl triglycerides) sera or plasma, or bilirubin (up to 40 mg/dl) containing sera or plasma. Nor have any interfering effects been observed with the use of anticoagulants (Citrate, EDTA, Heparine). However for practical reasons it is recommended that grossly hemolyzed or lipemic samples should be avoided.

Study results

Study population	n	n Pos	%
SLE	70	36	51.4
Rheumatoid arthritis	20	3	15.0
Normal human sera	100	2	2.0

		Clinical Diagnosis POS	NEG	
ORG 510	POS	36	5	
	NEG	34	115	
		70	120	190

Sensitivity: 51.4 %
Specificity: 95.8 %
Overall agreement: 79.5 %

LIMITATIONS OF THE PROCEDURE

This assay is a diagnostic aid. A definite clinical diagnosis should not be based on the results of a single test, but

should be made by the physician after all clinical and laboratory findings have been evaluated concerning the entire clinical picture of the patient. Also every decision for therapy should be taken individually.
The above pathological and normal reference ranges for antibodies in patient samples should be regarded as recommendations only. Each laboratory should establishe its own ranges according to ISO 15189 or other applicable laboratory guidelines.

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Notice to the user (European Union):
Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or the patient is established .

Change Control
Former version: *ORG 510_IFU_EN_QM113137_2013-12-16_1.2* Reason for revision: *Introduction electronic IFU on homepage*

1. Pipet **100 µl** calibrator, control or patient sample
   → Incubate for **30 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
2. Pipet **100 µl** enzyme conjugate
   → Incubate for **15 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
3. Pipet **100 µl** substrate solution
   → Incubate for **15 minutes** at room temperature
4. Add **100 µl** stop solution
   → Leave untouched for **5 minutes**
   → Read at **450 nm**

ORGENTEC

EG Konformitätserklärung

EC Declaration of Conformity

ORGENTEC Diagnostika GmbH
Carl-Zeiss-Straße 49-51, 55129 Mainz, GERMANY

Wir erklären in eigener Verantwortung, dass das ORGENTEC Produkt

We declare in our sole responsibility that the ORGENTEC product

ORG 511 Anti-RNP/Sm

zur quantitativen in-vitro-Bestimmung bestimmt ist und entsprechend Art. 9 Abs. Satz 1 der Europäischen Richtlinie 98/79/EG als „Sonstige Produkte" (non-A, non-B, keine Selbstanwendung) klassifiziert ist.

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Das Produkt stimmt mit den Grundlegenden Anforderungen und allen zutreffenden Bestimmungen der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998 über in-vitro-Diagnostika überein. Die Konformität zur Richtlinie wurde durch ein Konformitätsbewertungsverfahren nach Anhang III der Richtlinie festgestellt.

This product is conform with the essential requirements and meet the appropriate provisions of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. Conformity was proved by a conformity assessment procedure referred to in annex III of the directive.

Liste angewendeter Normen:

List of standards applied for CE marking:
EN ISO 13485, EN ISO 14971, EN ISO 18113, EN ISO 15223, EN ISO 23640, EN 13612.

ORGENTEC Diagnostika GmbH * ORGENTEC CE and ISO-approved * Carl-Zeiss-Str. 49-51, 55129 Mainz, GERMANY

Mainz, 2021-02-05

René Betz
Head of Regulatory Affairs

Gültig ab / Valid from 2021-02-05 bis / until 2024-02-28

Notification pursuant to §25 Abs. 3 Nr. 3 Medical Devices Act, MPG
Type: Reagent
EDMS 12-10-01-14-00
GMDN 55160

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511_3

ORG 511 Anti-RNP/Sm

INTENDED PURPOSE

Anti-RNP/Sm is an ELISA test system for the quantitative measurement of IgG class autoantibodies against RNP/Sm in human serum or plasma. This product is intended for professional in vitro diagnostic use only.

Antibodies against the RNP/Sm complex are useful in the diagnosis of mixed connective tissue disorder (MCTD, Sharp syndrome) and related autoimmune diseases. Antibodies against the 70 kDa protein of this complex are a very specific marker for Sharp syndrome. The Sm proteins are recognised by antibodies that may occur in cases of mixed connective tissue disorder and systemic lupus erythematosus. Evaluation of a test result should always take into account all clinical and laboratory diagnostic findings.

SYMBOLS USED ON LABELS

IVD	In vitro diagnostic medical device
	Manufacturer
REF	Catalogue number
Σ 96	Sufficient for 96 determinations
LOT	Batch code
	Use by
2°C 8°C	Temperature limitation
	Keep away from sunlight
	Do not reuse
	Date of manufacture
CE	CE marked according to 98/79/EC
	Consult instructions for use
511_3	Electronic Instruction For Use: version

MICROPLATE	Microplate
CALIBRATOR A	Calibrator
CALIBRATOR B	Calibrator
CALIBRATOR C	Calibrator
CALIBRATOR D	Calibrator
CALIBRATOR E	Calibrator
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CONTROL +	Control positive
CONTROL −	Control negative
DILUENT	Sample Buffer P
CONJUGATE	Enzyme Conjugate
TMB	TMB Substrate
STOP	Stop solution
WASH	Wash Buffer
RTU	Ready to use

PRINCIPLE OF THE TEST

Highly purified RNP/Sm is bound to microwells.
The determination is based on an indirect enzyme linked immune reaction with the following steps:
Specific antibodies in the patient sample bind to the antigen coated on the surface of the reaction wells. After incubation, a washing step removes unbound and unspecifically bound serum or plasma components. Subesquently added enzyme conjugate binds to the immobilized antibody-antigen-complexes. After incubation, a second washing step removes unbound enzyme conjugate. After addition of substrate solution the bound enzyme conjugate hydrolyses the substrate forming a blue coloured product. Addition of an acid stopps the reaction generating a yellow end-product. The intensity of the yellow color
correlates with the concentration of the antibody-antigen-complex and can be measured photometrically at 450 nm.

WARNINGS AND PRECAUTIONS

- All reagents of this kit are intended for professional in vitro diagnostic use only.
- Components containing human serum were tested and found negative for HBsAg, HCV, HIV1 and HIV2 by FDA approved methods. No test can guarantee the absence of HBsAg, HCV, HIV1 or HIV2, and so all human serum based reagents in this kit must be handled as though capable of transmitting infection.
- Bovine serum albumin (BSA) used in components has been tested for BSE and found negative.
- Avoid contact with the substrate TMB (3,3´,5,5´-Tetramethyl-benzidine).
- Stop solution contains acid, classifiaction is non-hazardous. Avoid contact with skin.
- Control, sample buffer and wash buffer contain sodium azide 0.09% as preservative. This concentration is classified as non-hazardous.
- Enzyme conjugate contains ProClin 300 0.05% as preservative. This concentration is classified as non-hazardous.

During handling of all reagents, controls and serum samples observe the existing regulations for laboratory safety regulations and good laboratory practice:

- First aid measures: In case of skin contact, immediately wash thoroughly with water and soap. Remove contaminated clothing and shoes and wash before reuse. If system fluid comes into contact with skin, wash thoroughly with water. After contact with the eyes carefully rinse the opened eye with running water for at least 10 minutes. Get medical attention if necessary.
- Personal precautions, protective equipment and emergency procedures:

Observe laboratory safety regulations. Avoid contact with skin and eyes. Do not swallow. Do not pipette by mouth. Do not eat, drink, smoke or apply makeup in areas where specimens or kit reagents are handled. When spilled, absorb with an inert material and put the spilled material in an appropriate waste disposal.

- Exposure controls / personal protection: Wear protective gloves of nitril rubber or natural latex. Wear protective glasses. Used according to intended use no dangerous reactions known.
- Conditions to avoid: Since substrate solution is light-sensitive. Store in the dark.
- For disposal of laboratory waste the national or regional legislation has to be observed.

Observe the guidelines for performing quality control in medical laboratories by assaying control sera.

CONTENTS OF THE KIT

ORG 511	Σ 96	Sufficient for 96 determinations
MICROPLATE	1	One divisible microplate consisting of 12 modules of 8 wells each. Ready to use. Color code on module
CALIBRATOR A	1x 1.5 ml	Calibrator A 0 U/ml, containing serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR B	1x 1.5 ml	Calibrator B 12.5 U/ml, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR C	1x 1.5 ml	Calibrator C 25 U/ml, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR D	1x 1.5 ml	Calibrator D 50 U/ml, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR E	1x 1.5 ml	Calibrator E 100 U/ml, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR F	1x 1.5 ml	Calibrator F 200 U/ml, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CONTROL +	1x 1.5 ml	Control positive, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
CONTROL −	1x 1.5 ml	Control negative, containing RNP/Sm antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
DILUENT	20 ml	Sample Buffer P, containing PBS, BSA, detergent, preservative sodium azide 0.09%, yellow, concentrate (5 x).
CONJUGATE	15 ml	Enzyme Conjugate containing anti-human IgG antibodies, HRP labelled; PBS, BSA, detergent, preservative PROCLIN 0.05%, light red. Ready to use.
TMB	15 ml	TMB Substrate; containing 3,3', 5,5'- Tetramethylbenzidin, colorless. Ready to use.
STOP	15 ml	Stop solution; contains acid. Ready to use.
WASH	20 ml	Wash Buffer, containing Tris, detergent, preservative sodium azide 0.09%; 50 x conc.
	1	Certificate of Analysis

MATERIALS REQUIRED

- Microplate reader capable of endpoint measurements at 450 nm; optional: reference filter at 620 nm
- Data reduction software
- Multi-channel dispenser or repeatable pipette for 100 µl
- Vortex mixer
- Pipettes for 10 µl, 100 µl and 1000 µl
- Laboratory timing device
- Distilled or deionised water
- Measuring cylinder for 1000 ml and 100 ml
- Plastic container for storage of the wash solution

This ELISA assay is suitable for use on open automated ELISA processors. Each assay has to be validated on the respective automated system. Detailed information is provided upon request.

SPECIMEN COLLECTION, STORAGE AND HANDLING

- Collect whole blood specimens using acceptable medical techniques to avoid hemolysis.
- Allow blood to clot and separate the serum or plasma by centrifugation.
- Test serum should be clear and non-hemolyzed. Contamination by hemolysis or lipemia should be avoided, but does not interfere with this assay.
- Specimens may be refrigerated at 2-8°C for up to five days or stored at -20°C up to six months.
- Avoid repetitive freezing and thawing of serum or plasma samples. This may result in variable loss of antibody activity.
- Testing of heat-inactivated sera is not recommended.

STORAGE AND STABILITY

- Store test kit at 2-8°C in the dark.
- Do not expose reagents to heat, sun, or strong light during storage and usage.
- Store microplate sealed and dessicated in the clip bag provided.
- Shelf life of the unopended test kit is 18 months from day of production. Unopened reagents are stable until expiration of the kit. See labels for individual batch.
- Diluted Wash Buffer and Sample Buffer are stable for at least 30 days when stored at 2-8°C. We recommend consumption on the same day.

PROCEDURAL NOTES

- Do not use kit components beyond their expiration dates.
- Do not interchange kit components from different lots and products.
- All materials must be at room temperature (20-28°C) prior to use.
- Prepare all reagents and samples. Once started, performe the test without interruption.
- Double determinations may be done. By this means pipetting errors may become obvious.
- Perform the assay steps only in the order indicated.
- Always use fresh sample dilutions.
- Pipette all reagents and samples into the bottom of the wells.
- To avoid carryover or contamination, change the pipette tip between samples and different kit controls.
- Wash microwells thoroughly and remove the last droplets of wash buffer.
- All incubation steps must be accurately timed.
- Do not re-use microplate wells.

PREPARATION OF REAGENTS

WASH

Dilute the contents of one vial of the buffered wash solution concentrate (50x) with distilled or deionised water to a final volume of 1000 ml prior to use.

DILUENT

Sample Buffer P: Prior to use dilute the contents (20 ml) of one vial of sample buffer 5x concentrate with distilled or deionised water to a final volume of 100 ml.

Preparation of samples

Dilute patient samples 1:100 before the assay: Put 990 µl of prediluted sample buffer in a polystyrene tube and add 10 µl of sample. Mix well. Note: Calibrators / Controls are ready to use and need not be diluted.

TEST PROCEDURE

Prepare enough microplate modules for all calibrators / controls and patient samples.

1. Pipette **100 µl** of calibrators, controls and prediluted patient samples into the wells.
   Incubate for **30 minutes** at room temperature (20-28 °C).
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
2. Dispense **100 µ**l of enzyme conjugate into each well.
   Incubate for **15 minutes** at room temperature.
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
3. Dispense **100 µ**l of TMB substrate solution into each well.
   Incubate for **15 minutes** at room temperature
4. **Add 100 µl** of stop solution to each well of the modules
   Incubate for **5 minutes** at room temperature.
   Read the optical density at 450 nm (reference 600-690nm) and calculate the results.
   The developed colour is stable for at least 30 minutes. Read during this time.

Example for a pipetting scheme:

	1	2	3	4	5	6	7	8	9	10	11	12
A	A	P1										
B	B	P2										
C	C	P3										
D	D											
E	E											
F	F											
G	C+											
H	C-											

P1, ... patient sample A-F calibrators C+, C- controls

VALIDATION

Test results are valid if the optical densities at 450 nm for calibrators / controls and the results for controls comply with the reference ranges indicated on the Certificate of Analysis enclosed in each test kit.
If these quality control criteria are not met the assay run is invalid and should be repeated.

CALCULATION OF RESULTS

For quantitative results plot the optical density of each calibrator versus the calibrator concentration to create a calibration curve. The concentration of patient samples may then be estimated from the calibration curve by interpolation.
Using data reduction software a 4-Parameter-Fit with lin-log coordinates for optical density and concentration is the data reduction method of choice.

PERFORMANCE CHARACTERISTICS

Calibration

The assay system is calibrated against the internationally recognized reference sera from CDC, Atlanta USA.

Measuring range

The calculation range of this ELISA assay is 0 - 200 U/ml

Expected values

In a normal range study with samples from healthy blood donors the following ranges have been established with this ELISA assay: Cut-off 25 U/ml

Interpretation of results

Negative:	< 15 U/ml
Borderline:	15 - 25 U/ml
Positive:	> 25 U/ml

Linearity

Patient samples containing high levels of specific antibody were serially diluted in sample buffer to demonstrate the dynamic range of the assay and the upper / lower end of linearity. Activity for each dilution was calculated from the calibration curve using a 4-Parameter-Fit with lin-log coordinates.

Sample	Dilution	Observed U/ml	Expected U/ml	O/E [%]
1	1:100	161.4	161.4	100
.	1:200	78.0	80.7	97
.	1:400	39.7	40.4	98
.	1:800	20.1	20.2	100
2	1:100	167.2	167.2	100
.	1:200	83.7	83.6	100
.	1:400	41.5	41.8	99
.	1:800	20.8	20.9	100

Limit of detection

Functional sensitivity was determined to be: 1 U/ml

Reproducibility

Intra-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 24 determinations in a single run. Results for precision-within-assay are shown in the table below.
Inter-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 6 determinations in 5 different runs. Results for run-to-run precision are shown in the table below.

Intra-Assay		
Sample	Mean U/ml	CV %
1	65.6	4.1
2	101.9	5.9
3	182.0	1.8

Inter-Assay		
Sample	Mean U/ml	CV %
1	33.3	4.2
2	109.0	3.1
3	176.8	2.9

Interfering substances

No interference has been observed with haemolytic (up to 1000 mg/dl) or lipemic (up to 3 g/dl triglycerides) sera or plasma, or bilirubin (up to 40 mg/dl) containing sera or plasma. Nor have any interfering effects been observed with the use of anticoagulants (Citrate, EDTA, Heparine). However for practical reasons it is recommended that grossly hemolyzed or lipemic samples should be avoided.

Study results

Study population	n	n Pos	%
SLE	70	37	52.9
MCTD	30	29	96.7
Rheumatoid arthritis	20	3	15.0
Normal human sera	100	2	2.0

		Clinical Diagnosis POS	NEG	
ORG 511	POS	66	5	
	NEG	34	115	
		100	120	220

Sensitivity: 66.0 %
Specificity: 95.8 %
Overall agreement: 82.3 %

LIMITATIONS OF THE PROCEDURE

This assay is a diagnostic aid. A definite clinical diagnosis should not be based on the results of a single test, but should be made by the physician after all clinical and laboratory findings have been evaluated concerning the entire clinical picture of the patient. Also every decision for therapy should be taken individually.

The above pathological and normal reference ranges for antibodies in patient samples should be regarded as recommendations only. Each laboratory should establishe its own ranges according to ISO 15189 or other applicable laboratory guidelines.

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Notice to the user (European Union):

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or the patient is established .

Change Control

Former version: *ORG 511_IFU_EN_QM113138_2013-12-16_1.2* Reason for revision: *Introduction electronic IFU on homepage*

1. Pipet **100 µl** calibrator, control or patient sample
   → Incubate for **30 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
2. Pipet **100 µl** enzyme conjugate
   → Incubate for **15 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
3. Pipet **100 µl** substrate solution
   → Incubate for **15 minutes** at room temperature
4. Add **100 µl** stop solution
   → Leave untouched for **5 minutes**
   → Read at **450 nm**

ORGENTEC

EG Konformitätserklärung

EC Declaration of Conformity

ORGENTEC Diagnostika GmbH
Carl-Zeiss-Straße 49-51, 55129 Mainz, GERMANY

Wir erklären in eigener Verantwortung, dass das ORGENTEC Produkt

We declare in our sole responsibility that the ORGENTEC product

ORG 548 Anti-MCV

zur quantitativen in-vitro-Bestimmung bestimmt ist und entsprechend Art. 9 Abs. Satz 1 der Europäischen Richtlinie 98/79/EG als „Sonstige Produkte" (non-A, non-B, keine Selbstanwendung) klassifiziert ist.

as intended for use in quantitative in vitro determination is classified as "Other Devices" (non-A, non-B, no self-testing device) *according to article 9 paragraph 1 sentence 1 of the European directive 98/79/EC.*

Das Produkt stimmt mit den Grundlegenden Anforderungen und allen zutreffenden Bestimmungen der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998 über in-vitro-Diagnostika überein. Die Konformität zur Richtlinie wurde durch ein Konformitätsbewertungsverfahren nach Anhang III der Richtlinie festgestellt.

This product is conform with the essential requirements and meet the appropriate provisions of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. Conformity was proved by a conformity assessment procedure referred to in annex III of the directive.

Liste angewendeter Normen:

List of standards applied for CE marking:
EN ISO 13485, EN ISO 14971, EN ISO 18113, EN ISO 15223, EN ISO 23640, EN 13612.

ORGENTEC Diagnostika GmbH
ORGENTEC
CE and ISO-approved
Carl-Zeiss-Str. 49-51, 55129 Mainz, GERMANY

Mainz, 2021-02-05

René Betz
Head of Regulatory Affairs

Gültig ab / Valid from 2021-02-05 bis / until 2024-02-28

Notification pursuant to §25 Abs. 3 Nr. 3 Medical Devices Act, MPG
Type: Reagent
EDMS 12-11-01-90-00
GMDN 62473

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548_5

ORG 548 Anti-MCV

INTENDED PURPOSE

Anti-MCV is an ELISA test system for the quantitative measurement of IgG class autoantibodies against mutated citrullinated vimentin (MCV) in human serum or plasma. This product is intended for professional in vitro diagnostic use only.

Measurement of anti-MCV antibodies contributes to early diagnosis of rheumatoid arthritis (RA), where anti-MCV antibody levels represent one parameter of a multi-criterion diagnostic process, encompassing both clinical and laboratory-based assessments.

SYMBOLS USED ON LABELS

Rx only	Applicable for U.S.A.: Prescription in vitro diagnostic product
For In Vitro Diagnostic Use	Applicable for U.S.A.: in vitro diagnostic product
IVD	In vitro diagnostic medical device
	Manufacturer
REF	Catalogue number
96	Sufficient for 96 determinations
LOT	Batch code
	Use by
2°C 8°C	Temperature limitation
	Keep away from sunlight
	Do not reuse
	Date of manufacture
CE	CE marked according to 98/79/EC
	Consult instructions for use
548_5	Electronic Instruction For Use: version

MICROPLATE	Microplate
CALIBRATOR A	Calibrator
CALIBRATOR B	Calibrator
CALIBRATOR C	Calibrator
CALIBRATOR D	Calibrator
CALIBRATOR E	Calibrator
CALIBRATOR F	Calibrator
CONTROL +	Control positive
CONTROL −	Control negative
DILUENT	Sample Buffer P
CONJUGATE	Enzyme Conjugate
TMB	TMB Substrate
STOP	Stop solution
WASH	Wash Buffer
RTU	Ready to use

PRINCIPLE OF THE TEST

Mutated citrullinated vimentin (MCV) is bound to microwells.

The determination is based on an indirect enzyme linked immune reaction with the following steps:
Specific antibodies in the patient sample bind to the antigen coated on the surface of the reaction wells. After incubation, a washing step removes unbound and unspecifically bound serum or plasma components. Subsequently added enzyme conjugate binds to the immobilized antibody-antigen-complexes. After incubation, a second washing step removes unbound enzyme conjugate. After addition of substrate solution the bound enzyme conjugate hydrolyses the substrate forming a blue coloured product. Addition of an acid stops the reaction generating a yellow end-product. The intensity of the yellow color
correlates with the concentration of the antibody-antigen-complex and can be measured photometrically at 450 nm.

WARNINGS AND PRECAUTIONS

- All reagents of this kit are intended for professional in vitro diagnostic use only.
- Components containing human serum were tested and found negative for HBsAg, HCV, HIV1 and HIV2 by FDA approved methods. No test can guarantee the absence of HBsAg, HCV, HIV1 or HIV2, and so all human serum based reagents in this kit must be handled as though capable of transmitting infection.
- Bovine serum albumin (BSA) used in components has been tested for BSE and found negative.
- Avoid contact with the substrate TMB (3,3´,5,5´-Tetramethyl-benzidine).
- Stop solution contains acid, classification is non-hazardous. Avoid contact with skin.
- Control, sample buffer and wash buffer contain sodium azide 0.09% as preservative. This concentration is classified as non-hazardous.
- Enzyme conjugate contains ProClin 300 0.05% as preservative. This concentration is classified as non-hazardous.

During handling of all reagents, controls and serum samples observe the existing regulations for laboratory safety regulations and good laboratory practice:

- First aid measures: In case of skin contact, immediately wash thoroughly with water and soap. Remove contaminated clothing and shoes and wash before reuse. If system fluid comes into contact with skin, wash thoroughly with water. After contact with the eyes carefully rinse the opened eye with running water for at least 10 minutes. Get medical attention if necessary.
- Personal precautions, protective equipment and emergency procedures:

Observe laboratory safety regulations. Avoid contact with skin and eyes. Do not swallow. Do not pipette by mouth. Do not eat, drink, smoke or apply makeup in areas where specimens or kit reagents are handled. When spilled, absorb with an inert material and put the spilled material in an appropriate waste disposal.

- Exposure controls / personal protection: Wear protective gloves of nitril rubber or natural latex. Wear protective glasses. Used according to intended use no dangerous reactions known.
- Conditions to avoid: Since substrate solution is light-sensitive. Store in the dark.
- For disposal of laboratory waste the national or regional legislation has to be observed.

Observe the guidelines for performing quality control in medical laboratories by assaying control sera.

CONTENTS OF THE KIT

ORG 548	▽96	Sufficient for 96 determinations
MICROPLATE	1	One divisible microplate consisting of 12 modules of 8 wells each. Ready to use. Product code on module: ***MCV***
CALIBRATOR A	1x 1.5 ml	Calibrator A 0 U/ml, containing serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR B	1x 1.5 ml	Calibrator B 20 U/ml, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR C	1x 1.5 ml	Calibrator C 40 U/ml, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR D	1x 1.5 ml	Calibrator D 100 U/ml, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR E	1x 1.5 ml	Calibrator E 300 U/ml, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR F	1x 1.5 ml	Calibrator F 1000 U/ml, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CONTROL +	1x 1.5 ml	Control positive, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
CONTROL −	1x 1.5 ml	Control negative, containing MCV antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
DILUENT	20 ml	Sample Buffer P, containing PBS, BSA, detergent, preservative sodium azide 0.09%, yellow, concentrate (5 x).
CONJUGATE	15 ml	Enzyme Conjugate containing anti-human IgG antibodies, HRP labelled; PBS, BSA, detergent, preservative PROCLIN 0.05%, light red. Ready to use.
TMB	15 ml	TMB Substrate; containing 3,3', 5,5'- Tetramethylbenzidin, colorless. Ready to use.
STOP	15 ml	Stop solution; contains acid. Ready to use.
WASH	20 ml	Wash Buffer, containing Tris, detergent, preservative sodium azide 0.09%; 50 x conc.

MATERIALS REQUIRED

- Microplate reader capable of endpoint measurements at 450 nm; optional: reference filter at 620 nm
- Data reduction software
- Multi-channel dispenser or repeatable pipette for 100 µl
- Vortex mixer
- Pipettes for 10 µl, 100 µl and 1000 µl
- Laboratory timing device
- Distilled or deionised water
- Measuring cylinder for 1000 ml and 100 ml
- Plastic container for storage of the wash solution

This ELISA assay is suitable for use on open automated ELISA processors. Each assay has to be validated on the respective automated system. Detailed information is provided upon request.

SPECIMEN COLLECTION, STORAGE AND HANDLING

- Collect whole blood specimens using acceptable medical techniques to avoid hemolysis.
- Allow blood to clot and separate the serum or plasma by centrifugation.
- Test serum should be clear and non-hemolyzed. Contamination by hemolysis or lipemia should be avoided, but does not interfere with this assay.
- Specimens may be refrigerated at 2-8°C for up to five days or stored at -20°C up to six months.
- Avoid repetitive freezing and thawing of serum or plasma samples. This may result in variable loss of antibody activity.
- Testing of heat-inactivated sera is not recommended.

STORAGE AND STABILITY

- Store test kit at 2-8°C in the dark.

- Do not expose reagents to heat, sun, or strong light during storage and usage.
- Store microplate sealed and dessicated in the clip bag provided.
- Shelf life of the unopended test kit is 18 months from day of production. Unopened reagents are stable until expiration of the kit. See labels for individual batch.
- Diluted Wash Buffer and Sample Buffer are stable for at least 30 days when stored at 2-8°C. We recommend consumption on the same day.

PROCEDURAL NOTES

- Do not use kit components beyond their expiration dates.
- Do not interchange kit components from different lots and products.
- All materials must be at room temperature (20-28°C) prior to use.
- Prepare all reagents and samples. Once started, performe the test without interruption.
- Double determinations may be done. By this means pipetting errors may become obvious.
- Perform the assay steps only in the order indicated.
- Always use fresh sample dilutions.
- Pipette all reagents and samples into the bottom of the wells.
- To avoid carryover or contamination, change the pipette tip between samples and different kit controls.
- Wash microwells thoroughly and remove the last droplets of wash buffer.
- All incubation steps must be accurately timed.
- Do not re-use microplate wells.

PREPARATION OF REAGENTS

WASH

Dilute the contents of one vial of the buffered wash solution concentrate (50x) with distilled or deionised water to a final volume of 1000 ml prior to use.

DILUENT

Sample Buffer P: Prior to use dilute the contents (20 ml) of one vial of sample buffer 5x concentrate with distilled or deionised water to a final volume of 100 ml.

Preparation of samples

Dilute patient samples 1:100 before the assay: Put 990 µl of prediluted sample buffer in a polystyrene tube and add 10 µl of sample. Mix well. Note: Calibrators / Controls are ready to use and need not be diluted.

TEST PROCEDURE

Prepare enough microplate modules for all calibrators / controls and patient samples.

1. Pipette **100 µl** of calibrators, controls and prediluted patient samples into the wells.
   Incubate for **30 minutes** at room temperature (20-28 °C).
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
2. Dispense **100 µ**l of enzyme conjugate into each well.
   Incubate for **15 minutes** at room temperature.
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
3. Dispense **100 µ**l of TMB substrate solution into each well.
   Incubate for **15 minutes** at room temperature
4. **Add 100 µl** of stop solution to each well of the modules
   Incubate for **5 minutes** at room temperature.
   Read the optical density at 450 nm (reference 600-690nm) and calculate the results.
   The developed colour is stable for at least 30 minutes. Read during this time.

Example for a pipetting scheme:

	1	2	3	4	5	6	7	8	9	10	11	12
A	A	P1										
B	B	P2										
C	C	P3										
D	D											
E	E											
F	F											
G	C+											
H	C-											

P1, ... patient sample A-F calibrators C+, C- controls

VALIDATION

Test results are valid if the optical densities at 450 nm for calibrators / controls and the results for controls comply with the reference ranges indicated on the Certificate of Analysis enclosed in each test kit.
If these quality control criteria are not met the assay run is invalid and should be repeated.

CALCULATION OF RESULTS

For quantitative results plot the optical density of each calibrator versus the calibrator concentration to create a calibration curve. The concentration of patient samples may then be estimated from the calibration curve by interpolation.
Using data reduction software a 4-Parameter-Fit with lin-log coordinates for optical density and concentration is the data reduction method of choice.

PERFORMANCE CHARACTERISTICS

CALIBRATION

This assay system is calibrated in relative arbitrary units, since no international reference preparation is available for this assay.

Measuring range

The calculation range of this ELISA assay is 0 - 1000 U/ml

Expected values

In a normal range study with samples from healthy blood donors the following ranges have been established with this ELISA assay: Cut-off 20 U/ml

Interpretation of results

Negative: < 20 U/ml
Positive: ≥ 20 U/ml

Linearity

Patient samples containing high levels of specific antibody were serially diluted in sample buffer to demonstrate the dynamic range of the assay and the upper / lower end of linearity. Activity for each dilution was calculated from the calibration curve using a 4-Parameter-Fit with lin-log coordinates.

Sample	Dilution	Observed U/ml	Expected U/ml	O/E [%]
1	1:100	882.8	882.8	100
.	1:200	386.0	441.4	87
.	1:400	205.2	220.7	93
.	1:800	110.7	110.4	100
.	1:1600	52.2	55.2	95
.	1:3200	23.4	27.6	85
2	1:100	932.1	932.1	100
.	1:200	486.0	466.1	104
.	1:400	250.1	233.0	107
.	1:800	126.6	116.5	109
.	1:1600	61.7	58.3	106
.	1:3200	28.2	29.1	97
3	1:100	727.9	727.9	100
.	1:200	362.4	364.0	100
.	1:400	178.2	182.0	98
.	1:800	85.7	91.0	94
.	1:1600	47.1	45.5	104
.	1:3200	19.2	22.7	85

Limit of detection

Functional sensitivity was determined to be: 1 U/ml

Reproducibility

Intra-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 24 determinations in a single run. Results for precision-within-assay are shown in the table below.
Inter-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 6 determinations in 5 different runs. Results for run-to-run precision are shown in the table below.

Intra-Assay		
Sample	Mean U/ml	CV %
1	22.7	6.2
2	118.8	6.4
3	548.1	4.6

Inter-Assay		
Sample	Mean U/ml	CV %
1	20.2	5.3
2	111.0	9.2
3	451.6	7.7

Interfering substances

No interference has been observed with haemolytic (up to 1000 mg/dl) or lipemic (up to 3 g/dl triglycerides) sera or plasma, or bilirubin (up to 40 mg/dl) containing sera or plasma. Nor have any interfering effects been observed with the use of anticoagulants (Citrate, EDTA, Heparine). However for practical reasons it is recommended that grossly hemolyzed or lipemic samples should be avoided.

Study results

Study population	n	n Pos	%
Rheumatoid arthritis	490	398	81.2
Other diseases	522	14	2.7
Normal human sera	234	1	0.4

		Clinical Diagnosis POS	NEG	
ORG 548	POS	398	15	
	NEG	92	741	
		490	756	1246

Sensitivity: 81.2 %
Specificity: 98.0 %
Overall agreement: 91.4 %

LIMITATIONS OF THE PROCEDURE

This assay is a diagnostic aid. A definite clinical diagnosis should not be based on the results of a single test, but should be made by the physician after all clinical and laboratory findings have been evaluated concerning the entire clinical picture of the patient. Also every decision for therapy should be taken individually.
The above pathological and normal reference ranges for antibodies in patient samples should be regarded as recommendations only. Each laboratory should establishe its own ranges according to ISO 15189 or other applicable laboratory guidelines.

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Notice to the user (European Union):
Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the

competent authority of the EU Member State in which the user and/or the patient is established .

Change Control

Former version: *ORG 548_IFU_DE_QM112972_2022-09-30_4* Reason for revision: *additional symbols*

INCUBATION SCHEME

1. Pipet **100 µl** calibrator, control or patient sample
   → Incubate for **30 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
2. Pipet **100 µl** enzyme conjugate
   → Incubate for **15 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
3. Pipet **100 µl** substrate solution
   → Incubate for **15 minutes** at room temperature
4. Add **100 µl** stop solution
   → Leave untouched for **5 minutes**
   → Read at **450 nm**

ORGENTEC

EG Konformitätserklärung

EC Declaration of Conformity

ORGENTEC Diagnostika GmbH
Carl-Zeiss-Straße 49-51, 55129 Mainz, GERMANY

Wir erklären in eigener Verantwortung, dass das ORGENTEC Produkt

We declare in our sole responsibility that the ORGENTEC product

ORG 549 Anti-C1q

zur quantitativen in-vitro-Bestimmung bestimmt ist und entsprechend Art. 9 Abs. Satz 1 der Europäischen Richtlinie 98/79/EG als „Sonstige Produkte" (non-A, non-B, keine Selbstanwendung) klassifiziert ist.

as intended for use in quantitative in vitro determination is classified as "Other Devices" (non-A, non-B, no self-testing device) *according to article 9 paragraph 1 sentence 1 of the European directive 98/79/EC.*

Das Produkt stimmt mit den Grundlegenden Anforderungen und allen zutreffenden Bestimmungen der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998 über in-vitro-Diagnostika überein. Die Konformität zur Richtlinie wurde durch ein Konformitätsbewertungsverfahren nach Anhang III der Richtlinie festgestellt.

This product is conform with the essential requirements and meet the appropriate provisions of the Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. Conformity was proved by a conformity assessment procedure referred to in annex III of the directive.

Liste angewendeter Normen:

List of standards applied for CE marking:
EN ISO 13485, EN ISO 14971, EN ISO 18113, EN ISO 15223, EN ISO 23640, EN 13612.

ORGENTEC Diagnostika GmbH * ORGENTEC CE and ISO approved * Carl-Zeiss-Str. 49-51, 55129 Mainz, GERMANY

Mainz, 2021-02-05

René Betz
Head of Regulatory Affairs

Gültig ab / Valid from 2021-02-05 bis / until 2024-02-28

Notification pursuant to §25 Abs. 3 Nr. 3 Medical Devices Act, MPG
Type: Reagent
EDMS 12-10-01-16-00
GMDN 53673

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549_3

ORG 549 Anti-C1q

INTENDED PURPOSE

Anti-C1q is an ELISA test system for the quantitative measurement of IgG class autoantibodies against C1q in human serum or plasma. This product is intended for professional in vitro diagnostic use only.

The test is used as an aid in the differential diagnosis of systemic autoimmune diseases with renal involvment, e.g. systemic lupus erythematosus, lupus nephritis. Evaluation of a test result should always take into account all clinical and laboratory diagnostic findings.

SYMBOLS USED ON LABELS

IVD	In vitro diagnostic medical device
	Manufacturer
REF	Catalogue number
96	Sufficient for 96 determinations
LOT	Batch code
	Use by
2°C 8°C	Temperature limitation
	Keep away from sunlight
	Do not reuse
	Date of manufacture
CE	CE marked according to 98/79/EC
	Consult instructions for use
549_3	Electronic Instruction For Use: version

MICROPLATE	Microplate
CALIBRATOR A	Calibrator
CALIBRATOR B	Calibrator
CALIBRATOR C	Calibrator
CALIBRATOR D	Calibrator
CALIBRATOR E	Calibrator
CALIBRATOR F	Calibrator
CONTROL +	Control positive
CONTROL −	Control negative
DILUENT	Sample Buffer P
CONJUGATE	Enzyme Conjugate
TMB	TMB Substrate
STOP	Stop solution
WASH	Wash Buffer
RTU	Ready to use

PRINCIPLE OF THE TEST

Highly purified human C1q is bound to microwells.
The determination is based on an indirect enzyme linked immune reaction with the following steps:
Specific antibodies in the patient sample bind to the antigen coated on the surface of the reaction wells. After incubation, a washing step removes unbound and unspecifically bound serum or plasma components. Subesquently added enzyme conjugate binds to the immobilized antibody-antigen-complexes. After incubation, a second washing step removes unbound enzyme conjugate. After addition of substrate solution the bound enzyme conjugate hydrolyses the substrate forming a blue coloured product. Addition of an acid stopps the reaction generating a yellow end-product. The intensity of the yellow color
correlates with the concentration of the antibody-antigen-complex and can be measured photometrically at 450 nm.

WARNINGS AND PRECAUTIONS

- All reagents of this kit are intended for professional in vitro diagnostic use only.
- Components containing human serum were tested and found negative for HBsAg, HCV, HIV1 and HIV2 by FDA approved methods. No test can guarantee the absence of HBsAg, HCV, HIV1 or HIV2, and so all human serum based reagents in this kit must be handled as though capable of transmitting infection.
- Bovine serum albumin (BSA) used in components has been tested for BSE and found negative.
- Avoid contact with the substrate TMB (3,3´,5,5´-Tetramethyl-benzidine).
- Stop solution contains acid, classifiaction is non-hazardous. Avoid contact with skin.
- Control, sample buffer and wash buffer contain sodium azide 0.09% as preservative. This concentration is classified as non-hazardous.
- Enzyme conjugate contains ProClin 300 0.05% as preservative. This concentration is classified as non-hazardous.

During handling of all reagents, controls and serum samples observe the existing regulations for laboratory safety regulations and good laboratory practice:

- First aid measures: In case of skin contact, immediately wash thoroughly with water and soap. Remove contaminated clothing and shoes and wash before reuse. If system fluid comes into contact with skin, wash thoroughly with water. After contact with the eyes carefully rinse the opened eye with running water for at least 10 minutes. Get medical attention if necessary.
- Personal precautions, protective equipment and emergency procedures:

Observe laboratory safety regulations. Avoid contact with skin and eyes. Do not swallow. Do not pipette by mouth. Do not eat, drink, smoke or apply makeup in areas where specimens or kit reagents are handled. When spilled, absorb with an inert material and put the spilled material in an appropriate waste disposal.

- Exposure controls / personal protection: Wear protective gloves of nitril rubber or natural latex. Wear protective glasses. Used according to intended use no dangerous reactions known.
- Conditions to avoid: Since substrate solution is light-sensitive. Store in the dark.
- For disposal of laboratory waste the national or regional legislation has to be observed.

Observe the guidelines for performing quality control in medical laboratories by assaying control sera.

CONTENTS OF THE KIT

ORG 549	Σ 96	Sufficient for 96 determinations
MICROPLATE	1	One divisible microplate consisting of 12 modules of 8 wells each. Ready to use. Product code on module: ***C1Q***
CALIBRATOR A	1x 1.5 ml	Calibrator A 0 U/ml, containing serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR B	1x 1.5 ml	Calibrator B 6.3 U/ml, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR C	1x 1.5 ml	Calibrator C 12.5 U/ml, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR D	1x 1.5 ml	Calibrator D 25 U/ml, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR E	1x 1.5 ml	Calibrator E 50 U/ml, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, NaN3 0.09%), yellow. Ready to use.
CALIBRATOR F	1x 1.5 ml	Calibrator F 100 U/ml, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use.
CONTROL +	1x 1.5 ml	Control positive, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
CONTROL −	1x 1.5 ml	Control negative, containing C1q antibodies in a serum/buffer matrix (PBS, BSA, detergent, NaN3 0.09%), yellow. Ready to use. The concentration is specified on the certificate of analysis.
DILUENT	20 ml	Sample Buffer P, containing PBS, BSA, detergent, preservative sodium azide 0.09%, yellow, concentrate (5 x).
CONJUGATE	15 ml	Enzyme Conjugate containing anti-human IgG antibodies, HRP labelled; PBS, BSA, detergent, preservative PROCLIN 0.05%, light red. Ready to use.
TMB	15 ml	TMB Substrate; containing 3,3', 5,5'- Tetramethylbenzidin, colorless. Ready to use.
STOP	15 ml	Stop solution; contains acid. Ready to use.
WASH	20 ml	Wash Buffer, containing Tris, detergent, preservative sodium azide 0.09%; 50 x conc.
	1	Certificate of Analysis

MATERIALS REQUIRED

- Microplate reader capable of endpoint measurements at 450 nm; optional: reference filter at 620 nm
- Data reduction software
- Multi-channel dispenser or repeatable pipette for 100 µl
- Vortex mixer
- Pipettes for 10 µl, 100 µl and 1000 µl
- Laboratory timing device
- Distilled or deionised water
- Measuring cylinder for 1000 ml and 100 ml
- Plastic container for storage of the wash solution

This ELISA assay is suitable for use on open automated ELISA processors. Each assay has to be validated on the respective automated system. Detailed information is provided upon request.

SPECIMEN COLLECTION, STORAGE AND HANDLING

- Collect whole blood specimens using acceptable medical techniques to avoid hemolysis.
- Allow blood to clot and separate the serum or plasma by centrifugation.
- Test serum should be clear and non-hemolyzed. Contamination by hemolysis or lipemia should be avoided, but does not interfere with this assay.
- Specimens may be refrigerated at 2-8°C for up to five days or stored at -20°C up to six months.
- Avoid repetitive freezing and thawing of serum or plasma samples. This may result in variable loss of antibody activity.
- Testing of heat-inactivated sera is not recommended.

STORAGE AND STABILITY

- Store test kit at 2-8°C in the dark.
- Do not expose reagents to heat, sun, or strong light during storage and usage.
- Store microplate sealed and dessicated in the clip bag provided.
- Shelf life of the unopended test kit is 18 months from day of production. Unopened reagents are stable until expiration of the kit. See labels for individual batch.
- Diluted Wash Buffer and Sample Buffer are stable for at least 30 days when stored at 2-8°C. We recommend consumption on the same day.

PROCEDURAL NOTES

- Do not use kit components beyond their expiration dates.
- Do not interchange kit components from different lots and products.
- All materials must be at room temperature (20-28°C) prior to use.
- Prepare all reagents and samples. Once started, performe the test without interruption.
- Double determinations may be done. By this means pipetting errors may become obvious.
- Perform the assay steps only in the order indicated.
- Always use fresh sample dilutions.
- Pipette all reagents and samples into the bottom of the wells.
- To avoid carryover or contamination, change the pipette tip between samples and different kit controls.
- Wash microwells thoroughly and remove the last droplets of wash buffer.
- All incubation steps must be accurately timed.
- Do not re-use microplate wells.

PREPARATION OF REAGENTS

WASH

Dilute the contents of one vial of the buffered wash solution concentrate (50x) with distilled or deionised water to a final volume of 1000 ml prior to use.

DILUENT

Sample Buffer P: Prior to use dilute the contents (20 ml) of one vial of sample buffer 5x concentrate with distilled or deionised water to a final volume of 100 ml.

Preparation of samples

Dilute patient samples 1:100 before the assay: Put 990 µl of prediluted sample buffer in a polystyrene tube and add 10 µl of sample. Mix well. Note: Calibrators / Controls are ready to use and need not be diluted.

TEST PROCEDURE

Prepare enough microplate modules for all calibrators / controls and patient samples.

1. Pipette **100 µl** of calibrators, controls and prediluted patient samples into the wells.
   Incubate for **30 minutes** at room temperature (20-28 °C).
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
2. Dispense **100 µ**l of enzyme conjugate into each well.
   Incubate for **15 minutes** at room temperature.
   Discard the contents of the microwells and **wash 3 times** with **300 µl** of wash solution.
3. Dispense **100 µ**l of TMB substrate solution into each well.
   Incubate for **15 minutes** at room temperature
4. **Add 100 µl** of stop solution to each well of the modules
   Incubate for **5 minutes** at room temperature.
   Read the optical density at 450 nm (reference 600-690nm) and calculate the results.
   The developed colour is stable for at least 30 minutes. Read during this time.

Example for a pipetting scheme:

	1	2	3	4	5	6	7	8	9	10	11	12
A	A	P1										
B	B	P2										
C	C	P3										
D	D											
E	E											
F	F											
G	C+											
H	C-											

P1, ... patient sample A-F calibrators C+, C- controls

VALIDATION

Test results are valid if the optical densities at 450 nm for calibrators / controls and the results for controls comply with the reference ranges indicated on the Certificate of Analysis enclosed in each test kit.
If these quality control criteria are not met the assay run is invalid and should be repeated.

CALCULATION OF RESULTS

For quantitative results plot the optical density of each calibrator versus the calibrator concentration to create a calibration curve. The concentration of patient samples may then be estimated from the calibration curve by interpolation. Using data reduction software a 4-Parameter-Fit with lin-log coordinates for optical density and concentration is the data reduction method of choice.

PERFORMANCE CHARACTERISTICS

Calibration

This assay system is calibrated in relative arbitrary units, since no international reference preparation is available for this assay.

Measuring range

The calculation range of this ELISA assay is 0 - 100 U/ml

Expected values

In a normal range study with samples from healthy blood donors the following ranges have been established with this ELISA assay: Cut-off 10 U/ml

Interpretation of results

Negative: < 10 U/ml
Positive: ≥ 10 U/ml

Linearity

Patient samples containing high levels of specific antibody were serially diluted in sample buffer to demonstrate the dynamic range of the assay and the upper / lower end of linearity. Activity for each dilution was calculated from the calibration curve using a 4-Parameter-Fit with lin-log coordinates.

Sample	Dilution	Observed U/ml	Expected U/ml	O/E [%]
1	1:100	88.4	88.4	100
	1:200	43.8	44.2	99
	1:400	22.7	22.1	103
	1:800	11.5	11.1	104
	1:1600	5.4	5.5	98
2	1:100	65.2	65.2	100
	1:200	32.1	32.6	98
	1:400	16.1	16.3	99
	1:800	7.9	8.2	97
	1:1600	3.7	4.1	91

Limit of detection

Functional sensitivity was determined to be: 0.5 U/ml

Reproducibility

Intra-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 24 determinations in a single run. Results for precision-within-assay are shown in the table below.
Inter-assay precision: Coefficient of variation (CV) was calculated for each of three samples from the results of 6 determinations in 5 different runs. Results for run-to-run precision are shown in the table below.

Intra-Assay		
Sample	Mean U/ml	CV %
1	25.2	3.7
2	58.6	3.0
3	75.4	2.9

Inter-Assay		
Sample	Mean U/ml	CV %
1	22.0	4.8
2	33.2	2.5
3	53.3	1.9

Interfering substances

No interference has been observed with haemolytic (up to 1000 mg/dl) or lipemic (up to 3 g/dl triglycerides) sera or plasma, or bilirubin (up to 40 mg/dl) containing sera or plasma. Nor have any interfering effects been observed with the use of anticoagulants (Citrate, EDTA, Heparine). However for practical reasons it is recommended that grossly hemolyzed or lipemic samples should be avoided.

Study results

Study population	n	n Pos	%
Lupus nephritis	34	29	85.3
Systemic lupus erythematosus	70	40	57.1
Other diseases	91	13	14.3
Normal human sera	74	4	5.4

		Clinical Diagnosis POS	NEG	
ORG 549	POS	69	17	
	NEG	35	148	
		104	165	269

Sensitivity: 66.3 %
Specificity: 89.7 %
Overall agreement: 80.7 %

LIMITATIONS OF THE PROCEDURE

This assay is a diagnostic aid. A definite clinical diagnosis should not be based on the results of a single test, but should be made by the physician after all clinical and laboratory findings have been evaluated concerning the entire clinical picture of the patient. Also every decision for therapy should be taken individually.
The above pathological and normal reference ranges for antibodies in patient samples should be regarded as recommendations only. Each laboratory should establishe its own ranges according to ISO 15189 or other applicable laboratory guidelines.

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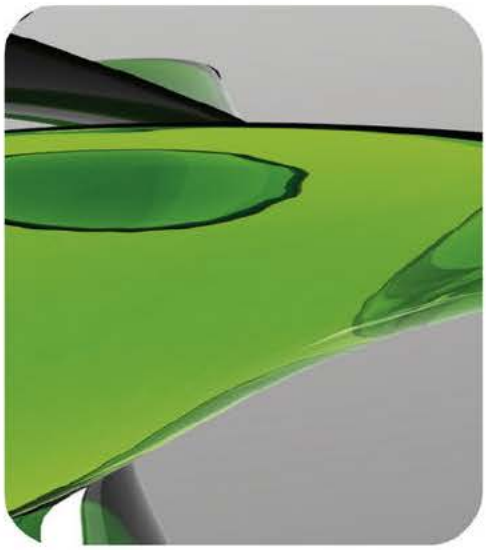
Notice to the user (European Union):
Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or the patient is established .

Change Control
Former version: *ORG 549_IFU_EN_QM113184_2013-12-16_1.2* Reason for revision: *Introduction electronic IFU on homepage*

1. Pipet **100 µl** calibrator, control or patient sample
   → Incubate for **30 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
2. Pipet **100 µl** enzyme conjugate
   → Incubate for **15 minutes** at room temperature
   → Discard the contents of the wells and wash 3 times with **300 µl** wash solution
3. Pipet **100 µl** substrate solution
   → Incubate for **15 minutes** at room temperature
4. Add **100 µl** stop solution
   → Leave untouched for **5 minutes**
   → Read at **450 nm**

AESKU.DIAGNOSTICS
THE DIAGNOSTIC TOOL THAT WORKS





AESKULISA®

THE DIAGNOSTIC TOOL THAT WORKS

INSTRUCTION MANUAL

AESKULISA SLA/LP

Ref 3704

DIN EN ISO 13485

Instruction Manual

Table of Contents

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1 Intended Use

AESKULISA SLA/LP is a solid phase enzyme immunoassay employing human recombinant SLA/LP for the quantitative and qualitative detection of IgG antibodies against soluble liver antigen (SLA) in human serum.

The assay is a tool for the diagnosis of autoimmune hepatitis (AIH).

2 Clinical Application and Principle of the Assay

Autoimmune hepatitis (AIH) is a chronic progressive liver disease of unknown origin that responds well to immunosuppressive therapy, but has a poor prognosis if untreated. Early and accurate diagnosis is therefore of great importance. AIH is characterized by histological features of periportal hepatitis in the absense of viral markers, by hypergammaglobulinemia and, in the majority of patients, by the presence of autoantibodies in serum. 70% of all patients have significant titres of anti-nuclear antibodies (ANA), smooth-muscle autoantibodies (SMA) or liver-kidney microsomal autoantibodies (LKM). These antibodies are of diagnostic value for AIH but not specific for the disease since they also occur in 10-15% of patients with viral hepatitis and other immune-mediated diseases. In contrast, antibodies to soluble liver antigen (SLA) and antibodies to a liver and pancreas antigen (LP) are the only to be specific for autoimmune hepatitis and are present in 20% of all AIH-patients, many of whom are negative for other autoantibodies. It was shown that anti-SLA and anti-LP are directed against the same antigen and thus are identical. The SLA/LP antigen cloned and sequenced in 2000 is a protein of unknown function, suggested to be an UGA-suppressor tRNA-associated protein.

ANA/SMA and anti-SLA positive patients share most clinical, biochemical, histological and prognostic features. Distinction of different subgroups according to autoantibody status is therefore clinically not helpful. However, testing for anti-SLA autoantibodies is very important for the diagnosis of AIH in many patients who are negative for other autoantibodies and may otherwise be misdiagnosed.

Principle of the test

Serum samples diluted 1:101 are incubated in the microplates coated with the specific antigen. Patient´s antibodies, if present in the specimen, bind to the antigen. The unbound fraction is washed off in the following step. Afterwards anti-human immunoglobulins conjugated to horseradish peroxidase (conjugate) are incubated and react with the antigen-antibody complex of the samples in the microplates. Unbound conjugate is washed off in the following step. Addition of TMB-substrate generates an enzymatic colorimetric (blue) reaction, which is stopped by diluted acid (color changes to yellow). The intensity of color formation from the chromogen is a function of the amount of conjugate bound to the antigen-antibody complex and this is proportional to the initial concentration of the respective antibodies in the patient sample.

3 Kit Contents

TO BE RECONSTITUTED				
Item	Quantity	Cap color	Solution color	Description / Contents
Sample Buffer (5x)	1 x 20ml	White	Yellow	5 x concentrated Tris, sodium chloride (NaCl), bovine serum albumin (BSA), sodium azide < 0.1% (preservative)
Wash Buffer (50x)	1 x 20ml	White	Green	50 x concentrated Tris, NaCl, Tween 20, sodium azide < 0.1% (preservative)
READY TO USE				
Item	Quantity	Cap color	Solution color	Description / Contents
Negative Control	1 x 1.5ml	Green	Colorless	Human serum (diluted), bovine serum albumin (BSA), sodium azide < 0.1% (preservative)
Positive Control	1 x 1.5ml	Red	Yellow	Human serum (diluted), bovine serum albumin (BSA), sodium azide < 0.1% (preservative)
Cut-off Calibrator	1 x 1.5ml	Blue	Yellow	Human serum (diluted), bovine serum albumin (BSA), sodium azide < 0.1% (preservative)
Calibrators	6 x 1.5ml	White	Yellow *	Concentration of each cal brator: 0, 3, 10, 30, 100, 300 U/ml. Human serum (diluted), bovine serum albumin (BSA), sodium azide < 0.1% (preservative)
Conjugate, IgG	1 x 15ml	Blue	Blue	Containing: Anti-human immunoglobulins conjugated to horseradish peroxidase, bovine serum albumin (BSA)
TMB Substrate	1 x 15ml	Black	Colorless	Stabilized tetramethy benzidine and hydrogen peroxide (TMB/H_2O_2)
Stop Solution	1 x 15ml	White	Colorless	1M Hydrochloric Acid
Microtiter plate	12 x 8 well strips	N/A	N/A	With breakaway microwells. Refer to paragraph 1 for coating.
* Color increasing with concentration				
MATERIALS REQUIRED, BUT NOT PROVIDED				
Microtiter plate reader 450 nm reading filter and recommended 620 nm reference filter (600-690 nm). Glass ware (cylinder 100-1000ml), test tubes for dilutions. Vortex mixer, precision pipettes (10, 100, 200, 500, 1000 µl) or adjustable multipipette (100-1000µl). Microplate washing device (300 µl repeating or multichannel pipette or automated system), adsorbent paper. Our tests are designed to be used with purified water according to the definition of the United States Pharmacopeia (USP 26 - NF 21) and the European Pharmacopeia (Eur.Ph. 4th ed.).				

4 Storage and Shelf Life

Store all reagents and the microplate at 2-8°C/35-46°F, in their original containers. Once prepared, reconstituted solutions are stable at 2-8°C/35-46°F for 1 month. Reagents and the microplate shall be used within the expiry date indicated on each component, only. Avoid intense exposure of TMB solution to light. Store microplates in designated foil, including the desiccant, and seal tightly.

5 Precautions of Use

5.1 Health hazard data

THIS PRODUCT IS FOR IN VITRO DIAGNOSTIC USE ONLY. Thus, only staff trained and specially advised in methods of in vitro diagnostics may perform the kit. Although this product is not considered particularly toxic or dangerous in conditions of the intended use, refer to the following for maximum safety:

Recommendations and precautions

This kit contains potentially hazardous components. Though kit reagents are not classified being irritant to eyes and skin we recommend to avoid contact with eyes and skin and wear disposable gloves.

WARNING ! Calibrators, Controls and Buffers contain sodium azide (NaN_3) as a preservative. NaN_3 may be toxic if ingested or adsorbed by skin or eyes. NaN_3 may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up. Please refer to decontamination procedures as outlined by CDC or other local/national guidelines.

Do not smoke, eat or drink when manipulating the kit. Do not pipette by mouth.

All human source material used for some reagents of this kit (controls, standards e.g.) has been tested by approved methods and found negative for HbsAg, Hepatitis C and HIV 1. However, no test can guarantee the absence of viral agents in such material completely. Thus handle kit controls, standards and patient samples as if capable of transmitting infectious diseases and according to national requirements.

The kit contains material of animal origin as stated in the table of contents, handle according to national requirements.

5.2 General directions for use

In case that the product information, including the labeling, is defective or incorrect please contact the manufacturer or the supplier of the test kit.

Do not mix or substitute Controls, Calibrators, Conjugates or microplates from different lot numbers. This may lead to variations in the results.

Allow all components to reach room temperature (20-32°C/68-89.6°F) before use, mix well and follow the recommended incubation scheme for an optimum performance of the test.

Incubation: We recommend test performance at 30°C/86°F for automated systems.

Never expose components to higher temperature than 37°C/ 98.6°F.

Always pipette substrate solution with brand new tips only. Protect this reagent from light. Never pipette conjugate with tips used with other reagents prior.

A definite clinical diagnosis should not be based on the results of the performed test only, 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.

6 Sample Collection, Handling and Storage

Use preferentially freshly collected serum samples. Blood withdrawal must follow national requirements. Do not use icteric, lipemic, hemolysed or bacterially contaminated samples. Sera with particles should be cleared by low speed centrifugation (<1000 x g). Blood samples should be collected in clean, dry and empty tubes.

After separation, the serum samples should be used during the first 8h, respectively stored tightly closed at 2-8°C/35-46°F up to 48h, or frozen at -20°C/-4°F for longer periods

7 Assay Procedure

7.1 Preparations prior to starting

Dilute concentrated reagents:

Dilute the concentrated sample buffer 1:5 with distilled water (e.g. 20 ml plus 80 ml).

Dilute the concentrated wash buffer 1:50 with distilled water (e.g. 20 ml plus 980 ml).

To avoid mistakes we suggest to mark the cap of the different calibrators.

Samples:

Dilute serum samples 1:101 with sample buffer (1x)

e.g. 1000 µl sample buffer (1x) + 10 µl serum. Mix well !

Washing:

Prepare 20 ml of diluted wash buffer (1x) per 8 wells or 200 ml for 96 wells

e.g. 4 ml concentrate plus 196 ml distilled water.

Automated washing:

Consider excess volumes required for setting up the instrument and dead volume of robot pipette.

Manual washing:

Discard liquid from wells by inverting the plate. Knock the microwell frame with wells downside vigorously on clean adsorbent paper. Pipette 300 µl of diluted wash buffer into each well, wait for 20 seconds. Repeat the whole procedure twice again.

Microplates:

Calculate the number of wells required for the test. Remove unused wells from the frame, replace and store in the provided plastic bag, together with desiccant, seal tightly (2-8°C/35-46°F).

7.2 Pipetting Scheme

We suggest pipetting calibrators, controls and samples as follows:

For *QUANTITATIVE* interpretation

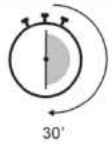
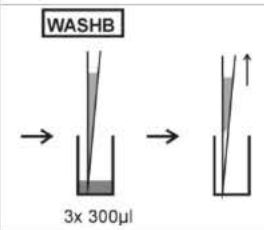
	1	2	3	4...
A	Cal A	Cal E	P1	
B	Cal A	Cal E	P1	
C	Cal B	Cal F	P2	
D	Cal B	Cal F	P2	
E	Cal C	PC	P3	
F	Cal C	PC	P3	
G	Cal D	NC	...	
H	Cal D	NC	...	

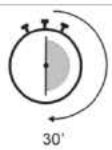
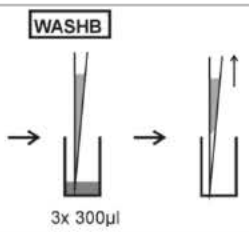
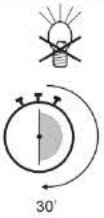
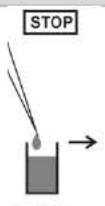
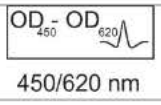
For *QUALITATIVE* interpretation

	1	2	3	4...
A	NC	P2		
B	NC	P2		
C	CC	P3		
D	CC	P3		
E	PC	...		
F	PC	...		
G	P1	...		
H	P1	...		

CalA: calibrator A
CalB: calibrator B
CalC: calibrator C
CalD: calibrator D
CalE: calibrator E
CalF: calibrator F
PC: positive control
NC: negative control
CC: cut-off calibrator
P1: patient 1
P2: patient 2
P3: patient 3

7.3 Test Steps

Step	*Description*
1.	Ensure preparations from step 7.1 above have been carried out prior to pipetting.
2.	Use the following steps in accordance with quantitative/ qualitative interpretation results desired:
	CONTROLS & SAMPLES
3.	 Pipette into the designated wells as described in chapter 7.2 above, 100 µl of either: a. Calibrators (CAL.A to CAL.F) for *QUANTITATIVE* or b. Cut-off Calibrator (CC) for *QUALITATIVE* interp. and 100 µl of each of the following: • Negative control (NC) and Positive control (PC), and • Patients diluted serum (P1, P2...)
4.	 Incubate for 30 minutes at 20-32°C/68-89.6°F.
5.	 Wash 3x with 300 µl washing buffer (diluted 1:50).

	CONJUGATE	
6.		Pipette 100 µl conjugate into each well.
7.		Incubate for 30 minutes at 20-32°C/68-89.6°F.
8.		Wash 3x with 300 µl washing buffer (diluted 1:50).
	SUBSTRATE	
9.		Pipette 100 µl TMB substrate into each well.
10.		Incubate for 30 minutes at 20-32°C/68-89.6°F, protected from intense light.
	STOP	
11.		Pipette 100 µl stop solution into each well, using the same order as pipetting the substrate.
12.		Incubate 5 minutes minimum.
13.		Agitate plate carefully for 5 sec.
14.		Read absorbance at 450 nm (recommended 450/620 nm) within 30 minutes.

8 Quantitative and Qualitative Interpretation

For **quantitative interpretation** establish the standard curve by plotting the **optical density (OD) of each calibrator (y-axis)** with respect to the corresponding concentration values in U/ml (x-axis). For best results we recommend log/lin coordinates and 4-Parameter Fit. From the OD of each sample, read the corresponding antibody concentrations expressed in U/ml.

Normal Range	Equivocal Range	Positive Results
< 12 U/ml	12 - 18 U/ml	>18 U/ml

Example of a standard curve

Do NOT use this example for interpreting patient´s result

Calibrators IgG	OD 450/620 nm	CV % (Variation)
0 U/ml	0.041	2.7
3 U/ml	0.178	2.4
10 U/ml	0.356	1.0
30 U/ml	0.725	0.9
100 U/ml	1.325	2.8
300 U/ml	2.070	1.6

Example of calculation

Patient	Replicate (OD)	Mean (OD)	Result (U/ml)
P 01	0.902/0.888	0.895	46.5
P 02	0.566/0.572	0.569	20.6

Samples above the highest calibrator range should be reported as >Max. They should be diluted as appropriate and re-assayed. Samples below calibrator range should be reported as < Min.
For lot specific data, see enclosed quality control leaflet. Medical laboratories might perform an in-house quality control by using own controls and/or internal pooled sera, as foreseen by national regulations.

Each laboratory should establish its own normal range based upon its own techniques, controls, equipment and patient population according to their own established procedures.

In case that the values of the controls do not meet the criteria the test is invalid and has to be repeated.

The following technical issues should be verified: Expiration dates of (prepared) reagents, storage conditions, pipettes, devices, photometer, incubation conditions and washing methods.

If the items tested show aberrant values or any kind of deviation or that the validation criteria are not met without explicable cause please contact the manufacturer or the supplier of the test kit.

For **qualitative interpretation** read the optical density of the cut-off calibrator and the patient samples. Compare patient´s OD with the OD of the cut-off calibrator. For qualitative interpretation we recommend to consider sera within a range of 20% around the cut-off value as equivocal. All samples with higher ODs are considered positive, samples with lower ODs are considered negative.

Negative:		**OD patient**	**<**	**0.8 x OD cut-off**		
Equivocal:	**0.8 x**	**OD cut-off**	**≤**	**OD patient**	**≤**	**1.2 x OD cut-off**
Positive:		**OD patient**	**>**	**1.2 x OD cut-off**		

9 Technical Data

Sample material:	serum
Sample volume:	10 µl of sample diluted 1:101 with 1x sample buffer
Total incubation time:	90 minutes at 20-32°C/68-89.6°F
Calibration range:	0-300 U/ml
Analytical sensitivity:	1.0 U/ml
Storage:	at 2-8°C/35-46°F use original vials only.
Number of determinations:	96 tests

10 Performance Data

10.1 Analytical sensitivity

Testing sample buffer 30 times on AESKULISA SLA/LP gave an analytical sensitivity of 1.0 U/ml.

10.2 Specificity and sensitivity

The microplate is coated with recombinant human liver antigen, SLA/LP.

No crossreactivities to other autoantigens have been found. The AESKULISA SLA/LP test exhibits a diagnostic specificity of 100%. The AESKULISA SLA/LP test exhibits a diagnostic sensitivity of 30%.

10.3 Linearity

Chosen sera have been tested with this kit and found to dilute linearly. However, due to the heterogeneous nature of human autoantibodies there might be samples that do not follow this rule.

Sample No.	Dilution Factor	Measured (U/ml)	Expected (U/ml)	Recovery (%)
1	1 / 100	156.0	155.0	100.7
	1 / 200	79.0	77.5	101.9
	1 / 400	41.0	38.5	105.7
	1 / 800	20.4	19.4	105.2
2	1 / 100	83.0	82.0	101.2
	1 / 200	43.0	41.0	102.4
	1 / 400	21.0	20.5	102.4
	1 / 800	11.0	10.3	106.8

10.4 Precision

To determine the precision of the assay, the variability (intra and inter-assay) was assessed by examining its reproducibility on three serum samples selected to represent a range over the standard curve.

Intra-assay		
Sample No.	**Mean (U/ml)**	**CV (%)**
1	160.0	2.4
2	85.0	2.8
3	20.8	3.1

Inter-assay		
Sample No.	**Mean (U/ml)**	**CV (%)**
1	154.0	1.8
2	80.0	2.8
3	18.4	3.4

10.5 Calibration

Due the lack of international reference calibration this assay is calibrated in arbitrary units (U/ml).

11 Literature

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IVD	- Diagnosi in vitro	- For in vitro diagnostic use
	- Pour diagnostic in vitro	- Para uso diagnóstico in vitro
	- In Vitro Diagnostikum	- In Vitro Διαγνωστικό μέσο
	- Para uso Diagnóstico in vitro	
REF	¨ Numero d'ordine	¨ Cataloge number
	¨ Référence Catalogue	¨ Numéro de catálogo
	¨ Bestellnummer	¨ Αριθμός παραγγελίας
	¨ Número de catálogo	
LOT	¨ Descrizione lotto	¨ Lot
	¨ Lot	¨ Lote
	¨ Chargen Bezeichnung	¨ Χαρακτηρισμός παρτίδας
	¨ Lote	
CE	¨ Conformità europea	¨ EC Declaration of Conformity
	¨ Déclaration CE de Conformité	¨ Declaración CE de Conformidad
	¨ Europäische Konformität	¨ Ευρωπαϊκή συμφωνία
	¨ Déclaracão CE de Conformidade	
Σ 96	¨ 96 determinazioni	¨ 96 tests
	¨ 96 tests	¨ 96 pruebas
	¨ 96 Bestimmungen	¨ 96 προσδιορισμοί
	¨ 96 Testes	
i	¨ Rispettare le istruzioni per l'uso	¨ See instructions for use
	¨ Voir les instructions d'utilisation	¨ Ver las instrucciones de uso
	¨ Gebrauchsanweisung beachten	¨ Λάβετε υπόψη τις οδηγίες χρήσης
	¨ Ver as instrucões de uso	
	¨ Da utilizzarsi entro	¨ Use by
	¨ Utilise avant le	¨ Utilizar antes de
	¨ Verwendbar bis	¨ Χρήση μέχρι
	¨ Utilizar antes de	
+2°C +8°C	¨ Conservare a 2-8°C	¨ Store at 2-8°C (35-46°F)
	¨ Conserver à 2-8°C	¨ Conservar a 2-8°C
	¨ Lagerung bei 2-8°C	¨ Φυλάσσεται στους 2-8°C
	¨ Conservar entre 2-8°C	
	¨ Prodotto da	¨ Manufactured by
	¨ Fabriqué par	¨ Fabricado por
	¨ Hergestellt von	¨ Κατασκευάζεται από
	¨ Fabricado por	
CO-CAL	¨ Calibratore cut-off	¨ Cut off Calibrator
	¨ Etalon Seuil	¨ Calibrador de cut-off
	¨ Grenzwert Kalibrator	¨ Οριακός ορός Αντιδραστήριο βαθμονόμησης
	¨ Calibrador de cut-off	
CON +	¨ Controllo positivo	¨ Positive Control
	¨ Contrôle Positif	¨ Control Positivo
	¨ Positiv Kontrolle	¨ Θετικός ορός ελέγχου
	¨ Controlo positivo	
CON −	¨ Controllo negativo	¨ Negative Control
	¨ Contrôle Négatif	¨ Control Negativo
	¨ Negativ Kontrolle	¨ Αρνητικός ορός ελέγχου
	¨ Controlo negativo	
CAL	¨ Calibratore	¨ Calibrator
	¨ Etalon	¨ Calibrador
	¨ Kalibrator	¨ Αντιδραστήριο βαθμονόμησης
	¨ Calibrador	
RC	¨ Recupero	¨ Recovery
	¨ Corrélation	¨ Recuperado
	¨ Wiederfindung	¨ Ανάκτηση
	¨ Recuperacão	
CONJ	¨ Coniugato	¨ Conjugate
	¨ Conjugé	¨ Conjugado
	¨ Konjugat	¨ Σύζευγμα
	¨ Conjugado	
MP	¨ Micropiastra rivestita	¨ Coated microtiter plate
	¨ Microplaque sensibilisée	¨ Microplaca sensibilizada
	¨ Beschichtete Mikrotiterplatte	¨ Επικαλυμμένη μικροπλάκα
	¨ Microplaca revestida	
WASHB 50x	¨ Tampone di lavaggio	¨ Wash buffer
	¨ Tampon de Lavage	¨ Solución de lavado
	¨ Waschpuffer	¨ Ρυθμιστικό διάλυμα πλύσης
	¨ Solucão de lavagem	
SUB	¨ Tampone substrato	¨ Substrate buffer
	¨ Substrat	¨ Tampón sustrato
	¨ Substratpuffer	¨ Ρυθμιστικό διάλυμα υποστρώματος
	¨ Substrato	
STOP	¨ Reagente bloccante	¨ Stop solution
	¨ Solution d'Arrêt	¨ Solución de parada
	¨ Stopreagenz	¨ Αντιδραστήριο διακοπής αντίδρασης
	¨ Solucão de paragem	
SB 5x	¨ Tampone campione	¨ Sample buffer
	¨ Tampon Echantillons	¨ Tampón Muestras
	¨ Probenpuffer	¨ Ρυθμιστικό διάλυμα δειγμάτων
	¨ Diluente de amostra	

AESKU.DIAGNOSTICS

Declaration of Conformity

CE

We

Aesku.Diagnostics GmbH & Co. KG

Mikroforum Ring 2, 55234 Wendelsheim, Deutschland / Germany

declare on our own responsibility that
the in-vitro diagnostic medical products from

Aesku.Diagnostics

listed in the annex
meet all the provisions of the Directive 98/79/EEC which apply to it.

Applied Standards:

DIN EN ISO 13485 (Certificate Number: MD 619745)

DIN EN 13612	DIN EN ISO 17050	DIN EN 23640	EN ISO 18113-1
DIN EN 13641	DIN EN ISO 17511	EN ISO 7010	EN ISO 18113-2
DIN EN ISO 14971	DIN EN 62366-1	EN 62304	EN ISO 18113-3
DIN EN ISO 15223-1	DIN EN ISO 19011	EN 61010-1	EN ISO 23640
			EN 61010-2-101

Conformity assessment procedure according to

Annex III
of Directive 98/79/EEC

The in-vitro diagnostics medical products of Aesku.Diagnostics are classified as

„other products“

according to the directive 98/79/EEC

This declaration of conformity loses its validity, if changes are made without approval of the manufacturer.

Wendelsheim, 2021-12-01

.....
Ort, Datum / place, date

.....
Dr. Torsten Matthias
CEO
Aesku.Diagnostics GmbH & Co. KG

Aesku.Diagnostics GmbH & Co.KG
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D-55234 Wendelsheim
Tel: (+49)-6734-96220
Fax: (+49)-6734-9622-2222

AESKU.DIAGNOSTICS

Annex to the Declaration of Conformity dated 2021-06-28

for

Aesku.Diagnostics

The above-mentioned declaration of conformity issued by Aesku.Diagnostics GmbH & Co. KG covers products with the following REFs:

Product	Test	REF	EDMA	Registration Code
	AESKULISA®			
AESKULISA® ANA-8S	ELISA 96 Tests	3100	12-10-01-01-00	DE/CA33/9001/001
AESKULISA® ANA-8Pro	ELISA 96 Tests	3101	12-10-01-01-00	DE/CA33/9001/002/1
AESKULISA® ENA-6S	ELISA 96 Tests	3102	12-10-01-02-00	DE/CA33/9001/003
AESKULISA® ENA-6Pro	ELISA 96 Tests	3103	12-10-01-90-00	DE/CA33/9001/004
AESKULISA® U1-70	ELISA 96 Tests	3104	12-10-01-14-00	DE/CA33/9001/005
AESKULISA® snRNP-C	ELISA 96 Tests	3105	12-10-01-14-00	DE/CA33/9001/006
AESKULISA® Sm	ELISA 96 Tests	3106	12-10-01-11-00	DE/CA33/9001/007
AESKULISA® SS-A	ELISA 96 Tests	3107	12-10-01-12-00	DE/CA33/9001/008
AESKULISA® SS-A-60	ELISA 96 Tests	3108	12-10-01-12-00	DE/CA33/9001/009
AESKULISA® SS-A-52	ELISA 96 Tests	3109	12-10-01-12-00	DE/CA33/9001/010
AESKULISA® SS-B	ELISA 96 Tests	3110	12-10-01-13-00	DE/CA33/9001/011
AESKULISA® Scl-70	ELISA 96 Tests	3111	12-10-01-10-00	DE/CA33/9001/012
AESKULISA® Cenp-B	ELISA 96 Tests	3112	12-10-01-15-00	DE/CA33/9001/013
AESKULISA® Jo-1	ELISA 96 Tests	3113	12-10-01-08-00	DE/CA33/9001/014
AESKULISA® Rib-P	ELISA 96 Tests	3114	12-10-90-20-00	DE/CA33/9001/015
AESKULISA® ANA HEp-2	ELISA 96 Tests	3115	12-10-01-01-00	DE/CA33/9001/026/1
AESKULISA® DANA-Pro	ELISA 96 Tests	3116	12-10-01-01-00	DE/CA33/9001/088
AESKULISA® PM-Scl	ELISA 96 Tests	3117	12-10-01-09-00	DE/CA33/9001/099
AESKULISA® ANA Hep-2 quantitative	ELISA 96 Tests	3119	12-10-01-01-00	DE/CA33/AES/2008/1
AESKULISA® Sclero-Pro	ELISA 96 Tests	3121	12-10-01-90-00	DE/CA33/9001/016
AESKULISA® Nucleo-h	ELISA 96 Tests	3130	12-10-90-18-00	DE/CA33/9001/017
AESKULISA® dsDNA-Check	ELISA 96 Tests	3140	12-10-01-05-00	DE/CA33/9001/018
AESKULISA® dsDNA-A	ELISA 96 Tests	3141	12-10-01-05-00	DE/CA33/9001/019
AESKULISA® dsDNA-G	ELISA 96 Tests	3142	12-10-01-05-00	DE/CA33/9001/020
AESKULISA® dsDNA-M	ELISA 96 Tests	3143	12-10-01-05-00	DE/CA33/9001/021
AESKULISA® ssDNA-Check	ELISA 96 Tests	3144	12-10-01-06-00	DE/CA33/9001/022

Product	Test	REF	EDMA	Registration Code
AESKULISA® ssDNA-A	ELISA 96 Tests	3145	12-10-01-06-00	DE/CA33/9001/023
AESKULISA® ssDNA-G	ELISA 96 Tests	3146	12-10-01-06-00	DE/CA33/9001/024
AESKULISA® ssDNA-M	ELISA 96 Tests	3147	12-10-01-06-00	DE/CA33/9001/025
AESKULISA® Histone-C	ELISA 96 Tests	3150	12-10-01-07-00	DE/CA33/9001/027
AESKULISA® Histone-H1	ELISA 96 Tests	3151	12-10-01-07-00	DE/CA33/9001/028
AESKULISA® Histone-H2A	ELISA 96 Tests	3152	12-10-01-07-00	DE/CA33/9001/029
AESKULISA® Histone-H2B	ELISA 96 Tests	3153	12-10-01-07-00	DE/CA33/9001/030
AESKULISA® Histone-H3	ELISA 96 Tests	3154	12-10-01-07-00	DE/CA33/9001/031
AESKULISA® Histone-H4	ELISA 96 Tests	3155	12-10-01-07-00	DE/CA33/9001/032
AESKULISA® Rf-Check	ELISA 96 Tests	3160	12-11-01-10-00	DE/CA33/9001/033
AESKULISA® Rf-AGM	ELISA 96 Tests	3161	12-11-01-10-00	DE/CA33/9001/034
AESKULISA® alpha-Fodrin-A	ELISA 96 Tests	3162	12-10-90-90-00	DE/CA33/9001/035
AESKULISA® alpha-Fodrin-G	ELISA 96 Tests	3163	12-10-90-90-00	DE/CA33/9001/036
AESKULISA® alpha-Fodrin-Check	ELISA 96 Tests	3164	12-10-90-90-00	DE/CA33/9001/091
AESKULISA® RA/CP-Detect	ELISA 96 Tests	3165	12-11-01-10-00	DE/CA33/9001/098/2
AESKULISA® CCP	ELISA 96 Tests	3166	12-11-01-90-00	DE/CA33/AES/2007/7
AESKULISA® MMP-3	ELISA 96 Tests	3168	12-11-01-90-00	DE/CA33/AES/2010/10/2
AESKULISA® MMP-3	ELISA 96 Tests	3171	12-11-01-90-00	DE/CA33/AES/2016/1
AESKULISA® SpA Detect	ELISA 96 Tests	3190	12-11-01-90-00	DE/CA33/AES/2016/6/1
AESKULISA® Cardiolipin-Check	ELISA 96 Tests	3202	12-10-90-01-00	DE/CA33/9001/049
AESKULISA® Cardiolipin-A	ELISA 96 Tests	3203	12-10-90-01-00	DE/CA33/9001/050
AESKULISA® Cardiolipin-GM	ELISA 96 Tests	3204	12-10-90-01-00	DE/CA33/9001/051
AESKULISA® ß2-Glyco-A	ELISA 96 Tests	3205	12-10-90-04-00	DE/CA33/9001/053
AESKULISA® ß2-Glyco-GM	ELISA 96 Tests	3206	12-10-90-04-00	DE/CA33/9001/054
AESKULISA® Serine-GM	ELISA 96 Tests	3207	12-10-90-03-00	DE/CA33/9001/055
AESKULISA® Inositol-GM	ELISA 96 Tests	3208	13-02-06-01-00	DE/CA33/9001/056/1
AESKULISA® Ethanolamine-GM	ELISA 96 Tests	3209	13-02-06-01-00	DE/CA33/9001/083
AESKULISA® Prothrombin-A	ELISA 96 Tests	3210	12-10	DE/CA33/9001/038
AESKULISA® Prothrombin-Check	ELISA 96 Tests	3211	13-02-06-01-00	DE/CA33/9001/103/1
AESKULISA® Choline-GM	ELISA 96 Tests	3212	13-02-06-01-00	DE/CA33/9001/102/1
AESKULISA® Thrombin-A	ELISA 96 Tests	3213	12-10-90-90-00	DE/CA33/9001/041/1
AESKULISA® Sphingomyelin-GM	ELISA 96 Tests	3214	13-02-06-01-00	DE/CA33/9001/100/1
AESKULISA® ß2-Glyco-Check	ELISA 96 Tests	3215	12-10-90-04-00	DE/CA33/9001/089
AESKULISA® Phospholipid-Screen	ELISA 96 Tests	3216	13-02-06-01-00	DE/CA33/9001/081/1
AESKULISA® Phospholipid-Screen-A	ELISA 96 Tests	3219	13-02-06-01-00	DE/CA33/9001/045/1
AESKULISA® Phospholipid-8Pro-A	ELISA 96 Tests	3222	13-02-06-01-00	DE/CA33/9001/048/1
AESKULISA® Serine-Prothrombin-Check	ELISA 96 Tests	3223	13-02-06-01-00	DE/CA33/9001/090/1

Product	Test	REF	EDMA	Registration Code
AESKULISA® Phospholipid-Screen-GM	ELISA 96 Tests	3224	13-02-06-01-00	DE/CA33/9001/082/1
AESKULISA® Thrombin-Check	ELISA 96 Tests	3225	12-10-90-90-00	DE/CA33/9001/080/1
AESKULISA® Serine-Prothrombin-GM	ELISA 96 Tests	3226	13-02-06-01-00	DE/CA33/9001/090/1
AESKULISA® Serine-Prothrombin-A	ELISA 96 Tests	3227	13-02-06-01-00	DE/CA33/9001/090/1
AESKULISA® Thrombin-GM	ELISA 96 Tests	3228	12-10-90-90-00	DE/CA33/9001/086/1
AESKULISA® Prothrombin-GM	ELISA 96 Tests	3229	12-10-90-90-00	DE/CA33/9001/092/1
AESKULISA® Thrombo-Profile	ELISA 96 Tests	3230	13-02-06-01-00	DE/CA33/9001/085/1
AESKULISA® Phosphatidic acid-GM	ELISA 96 Tests	3231	13-02-06-01-00	DE/CA33/9001/084/2
AESKULISA® Phospholipid-8Pro-GM	ELISA 96 Tests	3232	13-02-06-01-00	DE/CA33/9001/087/1
AESKULISA® APS-Profile-GM	ELISA 96 Tests	3234	13-02-06-01-00	DE/CA33/9001/110/1
AESKULISA® Laminin	ELISA 96 Tests	3235	12-10-90-90-00	DE/CA33/9001/112
AESKULISA® Ethanolamine-A	ELISA 96 Tests	3236	13-02-06-01-00	DE/CA33/AES/9001/116/1
AESKULISA® Annexin V-GM	ELISA 96 Tests	3240	12-10-90-90-00	DE/CA33/9001/097
AESKULISA® Cardiolipin-GM	ELISA 96 Tests	3244	12-10-90-01-00	DE/CA33/9001/052
AESKULISA® Glycerol-A	ELISA 96 Tests	3254	13-02-06-01-00	DE/CA33/AES/2007/2
AESKULISA® Glycerol-GM	ELISA 96 Tests	3255	13-02-06-01-00	DE/CA33/AES/2007/2
AESKULISA® HiT II	ELISA 96 Tests	3290	13-02-06-90-00	DE/CA33/AES/2007/5/1
AESKULISA® HiT II Check	ELISA 96 Tests	3291	13-02-06-90-00	DE/CA33/AES/2007/5/1
AESKULISA® ANCA-Pro	ELISA 96 Tests	3301	12-10-01-03-00	DE/CA33/9001/101/1
AESKULISA® PR3 sensitive	ELISA 96 Tests	3302	12-10-90-10-00	DE/CA33/9001/057
AESKULISA® MPO	ELISA 96 Tests	3303	12-10-90-09-00	DE/CA33/9001/058
AESKULISA® BPI	ELISA 96 Tests	3304	12-10-01-03-00	DE/CA33/9001/101/1
AESKULISA® Elastase	ELISA 96 Tests	3305	12-10-01-03-00	DE/CA33/9001/060/1
AESKULISA® Cathepsin G	ELISA 96 Tests	3306	12-10-01-03-00	DE/CA33/9001/061/1
AESKULISA® Lactoferrin	ELISA 96 Tests	3307	12-10-01-03-00	DE/CA33/9001/101/1
AESKULISA® Lysozyme	ELISA 96 Tests	3308	12-10-01-03-00	DE/CA33/9001/101/1
AESKULISA® GBM	ELISA 96 Tests	3309	12-10-90-15-00	DE/CA33/9001/062
AESKULISA® Vasculitis-Screen	ELISA 96 Tests	3323	12-10-01-03-00	DE/CA33/9001/063/1
AESKULISA® a-Tg	ELISA 96 Tests	3400	12-04-01-08-00	DE/CA33/9001/064
AESKULISA® a-TPO	ELISA 96 Tests	3401	12-10-03-01-00	DE/CA33/9001/065
AESKULISA® Tg	ELISA 96 Tests	3402	12-10-03-04-00	DE/CA33/9001/066
AESKULISA® Gliadin-Check	ELISA 96 Tests	3500	12-10-90-06-00	DE/CA33/AES/9001/115
AESKULISA® Glia-A	ELISA 96 Tests	3501	12-10-90-06-00	DE/CA33/9001/067
AESKULISA® Glia-G	ELISA 96 Tests	3502	12-10-90-06-00	DE/CA33/9001/068
AESKULISA® tTg-A New Generation	ELISA 96 Tests	3503	12-10-90-22-00	DE/CA33/9001/069/1
AESKULISA® tTg-G New Generation	ELISA 96 Tests	3504	12-10-90-22-00	DE/CA33/9001/070/1
AESKULISA® ASCA-A	ELISA 96 Tests	3507	12-10-90-19-00	DE/CA33/9001/072

Product	Test	REF	EDMA	Registration Code
AESKULISA® ASCA-G	ELISA 96 Tests	3508	12-10-90-19-00	DE/CA33/9001/073
AESKULISA® Crohn´s-Check	ELISA 96 Tests	3509	12-10-90-19-00	DE/CA33/9001/074/1
AESKULISA® CeliCheck New Generation	ELISA 96 Tests	3510	12-10-90-22-00	DE/CA33/9001/071/1
AESKULISA® Parietal Cell	ELISA 96 Tests	3511	12-10-90-11-00	DE/CA33/9001/113
AESKULISA® Intrinsic Factor	ELISA 96 Tests	3512	12-10-90-11-00	DE/CA33/AES/9001/114/1
AESKULISA® DGP-A	ELISA 96 Tests	3513	12-10-90-06-00	DE/CA33/AES/2010/1
AESKULISA® DGP-G	ELISA 96 Tests	3514	12-10-90-06-00	DE/CA33/AES/2010/1
AESKULISA® DGP-Check	ELISA 96 Tests	3515	12-10-90-06-00	DE/CA33/AES/2010/8
AESKULISA® tTg-GA New Generation	ELISA 96 Tests	3516	12-10-90-22-00	DE/CA33/AES/2010/15
AESKULISA® DGP-GA	ELISA 96 Tests	3517	12-10-90-06-00	DE/CA33/AES/2010/14
AESKULISA® mTg neo-epitope Check	ELISA 96 Tests	3520	12-10-90-90-00	DE/CA33/AES/2019/28
AESKULISA® Insulin	ELISA 96 Tests	3601	12-06-01-04-00	DE/CA33/9001/078/1
AESKULISA® LC-1	ELISA 96 Tests	3702	12-10-90-17-00	DE/CA33/9001/075/1
AESKULISA® LKM-1	ELISA 96 Tests	3703	12-10-90-08-00	DE/CA33/9001/076
AESKULISA® SLA/LP	ELISA 96 Tests	3704	12-10-90-17-00	DE/CA33/9001/079
AESKULISA® AMA-M2-G	ELISA 96 Tests	3705	12-10-90-02-00	DE/CA33/9001/077
AESKULISA® AMA-M2-M	ELISA 96 Tests	3706	12-10-90-02-00	DE/CA33/9001/111
AESKULISA® AMA-M2-Check	ELISA 96 Tests	3707	12-10-90-02-00	DE/CA33/9001/111
AESKULISA® ß-2 Microglobulin	ELISA 96 Tests	3801	12-03-90-02-00	DE/CA33/9001/096
AESKULISA® Borrelia-G	ELISA 96 Tests	3802	15-01-06-05-00	DE/CA33/AES/2006/16
AESKULISA® Borrelia-M	ELISA 96 Tests	3803	15-01-06-06-00	DE/CA33/AES/2006/17
AESKULISA® 25OH Vitamin D	ELISA 96 Tests	3810	12-06-03-10-00	DE/CA33/AES/2013/1/1
AESKULISA® Protein C	ELISA 96 Tests	3901	13-02-06-08-00	DE/CA33/AES-2007/4
AESKULISA® Protein S	ELISA 96 Tests	3902	13-02-06-09-00	DE/CA33/AES/2007/3
AESKULISA® Free Protein S	ELISA 96 Tests	3903	13-02-06-09-00	DE/CA33/AES/2008/2
AESKULISA® Herpes Simplex Virus 1/2 IgG	ELISA 96 Tests	6042	15-04-03-05-00	DE/CA33/AES/2019/2
AESKULISA® Herpes Simplex Virus 1/2 IgM	ELISA 96 Tests	6043	15-04-03-06-00	DE/CA33/AES/2019/29
AESKULISA® Herpes Simplex Virus 1 (gG1) IgG	ELISA 96 Tests	6045	15-04-03-08-00	DE/CA33/AES/2019/3
AESKULISA® Herpes Simplex Virus 2 (gG2) IgG	ELISA 96 Tests	6048	15-04-03-11-00	DE/CA33/AES/2019/4
AESKULISA® Varicella Zoster Virus IgA	ELISA 96 Tests	6051	15-04-80-10-00	DE/CA33/AES/2019/17
AESKULISA® Varicella Zoster Virus IgG	ELISA 96 Tests	6052	15-04-80-10-00	DE/CA33/AES/2019/16
AESKULISA® Varicella Zoster Virus IgM	ELISA 96 Tests	6053	15-04-80-10-00	DE/CA33/AES/2019/15
AESKULISA® Parvovirus B19 IgG	ELISA 96 Tests	6062	15-04-80-09-00	DE/CA33/AES/2018/1
AESKULISA® Parvovirus B19 IgM	ELISA 96 Tests	6063	15-04-80-09-00	DE/CA33/AES/2018/2
AESKULISA® Measles Virus IgG	ELISA 96 Tests	6072	15-04-80-07-00	DE/CA33/AES/2019/30
AESKULISA® Measles Virus IgM	ELISA 96 Tests	6073	15-04-80-07-00	DE/CA33/AES/2019/31
AESKULISA Clostridium tetani IgG	ELISA 96 Tests	6102	15-01-90-09-00	DE/CA33/AES/2021/1

Product	Test	REF	EDMA	Registration Code
AESKULISA® SARS-CoV-2 NP IgA	ELISA 96 Tests	6121	15-04-08-90-00	DE/CA33/AES/2020/1
AESKULISA® SARS-CoV-2 NP IgG	ELISA 96 Tests	6122	15-04-08-90-00	DE/CA33/AES/2020/2
AESKULISA® SARS-CoV-2 NP IgM	ELISA 96 Tests	6123	15-04-08-90-00	DE/CA33/AES/2020/3
AESKULISA® SARS-CoV-2 S1 IgA	ELISA 96 Tests	6124	15-04-80-90-00	DE/CA33/AES/2020/4
AESKULISA® SARS-CoV-2 S1 IgG	ELISA 96 Tests	6125	15-04-80-90-00	DE/CA33/AES/2020/5
AESKULISA® SARS-CoV-2 S1 IgM	ELISA 96 Tests	6126	15-04-80-90-00	DE/CA33/AES/2020/6
AESKU.RAPID SARS-CoV-2 rapid test				
AESKU.RAPID SARS-CoV-2 rapid test	20 Tests	840001	15-04-80-90-00	DE/CA33/AES/2020/7
AESKU.RAPID SARS-CoV-2 rapid test	5 Tests	840003	15-04-80-90-00	DE/CA33/AES/2020/7
AESKU.RAPID SARS-CoV-2 rapid test	2 Tests	840005	15-04-80-90-00	DE/CA33/AES/2020/7
AESKU.RAPID SARS-CoV-2 rapid test	1 Test	840007	15-04-80-90-00	DE/CA33/AES/2020/7
AESKU.COLLECT DBS	Sampling Kit	69610069	26-09	DE/CA33/AES/2021/2
AESKU.COVID19 CHECK	Sampling Kit	861002	26-09	DE/CA33/AES/2021/2
AESKUCARE®				
AESKUCARE® Allergy ONE	ELISA 1 Test	820101	12-02-01-06-00	DE/CA33/AES/2019/25
AESKUCARE® Allergy TWO	ELISA 1 Test	820102	12-02-01-06-00	DE/CA33/AES/2019/25/1
AESKUCARE® Allergy THREE	ELISA 1 Test	820201	12-02-01-06-00	DE/CA33/AES/2019/25/1
AESKUCARE® Allergy FOUR	ELISA 1 Test	820301	12-02-01-06-00	DE/CA33/AES/2019/25/1
AESKUCARE® Food Intolerance ONE	ELISA 1 Test	830101	12-01-01-06-00	DE/CA33/AES/2019/26
AESKUBLOTS®				
AESKUBLOTS® ANA-17 Pro	BLOT 24 Tests	4001	12-10-01-90-00	DE/CA33/AES/2012/1
AESKUBLOTS® Vasculitis Pro	BLOT 24 Tests	4002	12-10-01-03-00	DE/CA33/AES/2012/4
AESKUBLOTS® Myositis Pro	BLOT 24 Tests	4003	12-10-01-90-00	DE/CA33/AES/2012/3
AESKUBLOTS® Liver Pro	BLOT 24 Tests	4004	12-10-90-17-00	DE/CA33/AES/2012/5
AESKUBLOTS® Gastro Pro	BLOT 24 Tests	4005	12-10-90-90-00	DE/CA33/AES/2012/6
AESKUBLOTS® Borrelia-G	BLOT 24 Tests	4006	15-01-06-05-00	DE/CA33/AES/2012/7
AESKUBLOTS® Borrelia-M	BLOT 24 Tests	4007	15-01-06-06-00	DE/CA33/AES/2012/8
AESKUBLOTS® ANA-17 comp	BLOT 24 Tests	4008	12-10-01-90-00	DE/CA33/AES/2017/1
AESKUBLOTS® Allergy ONE	BLOT 24 Tests	421001	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy TWO	BLOT 24 Tests	421002	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy THREE	BLOT 24 Tests	421003	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy FOUR	BLOT 24 Tests	421004	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy FIVE	BLOT 24 Tests	421005	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy SIX	BLOT 24 Tests	421006	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy SEVEN	BLOT 24 Tests	421407	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy EIGHT	BLOT 24 Tests	421408	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy NINE	BLOT 24 Tests	421009	12-02-01-06-00	DE/CA33/AES/2019/5/1

Product	Test	REF	EDMA	Registration Code
AESKUBLOTS® Allergy TEN	BLOT 24 Tests	421010	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy ELEVEN	BLOT 24 Tests	421411	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy TWELVE	BLOT 24 Tests	421412	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Allergy THIRTEEN	BLOT 24 Tests	421413	12-02-01-06-00	DE/CA33/AES/2019/5/1
AESKUBLOTS® Food Intolerance ONE	BLOT 24 Tests	431401	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance TWO	BLOT 24 Tests	431402	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance THREE	BLOT 24 Tests	431403	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance FOUR	BLOT 24 Tests	431404	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance FIVE	BLOT 24 Tests	431405	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance SIX	BLOT 24 Tests	431406	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUBLOTS® Food Intolerance SEVEN	BLOT 24 Tests	431407	12-01-01-06-00	DE/CA33/AES/2019/18/1
AESKUSLIDES®				
AESKUSLIDES® ANA HEp-2	KIT 120 Tests	51.100	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® ANA HEp-2 Bulk Kit	KIT 600 Tests	51.100.Bulk5	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® ANA HEp-2	KIT 120 Tests	51.101	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® ANA HEp-2 Bulk Kit	KIT 600 Tests	51.101.Bulk5	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® EMA IgA	KIT 50 Tests	512.050	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® EMA IgG	KIT 50 Tests	512.060	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® EMA IgA	KIT 100 Tests	512.100	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® EMA IgG	KIT 100 Tests	512.101	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® rLKS wrapped	KIT 50 Tests	517.050	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® rLKS separated	KIT 50 Tests	517.051	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® rLKS separated	KIT 100 Tests	517.100	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® rLKS wrapped	KIT 100 Tests	517.101	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® mLKS separated	KIT 50 Tests	518.050	12-10-90-90-00	DE/CA33/9001/108/2
AESKUSLIDES® mLKS separated	KIT 100 Tests	518.100	12-10-90-90-00	DE/CA33/9001/108/2
AESKUSLIDES® nDNA (Crithidia luciliae)	KIT 100 Tests	53.100	12-10-01-05-00	DE/CA33/9001/105/1
AESKUSLIDES® ANCA Ethanol	KIT 60 Tests	54.050	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Formalin	KIT 60 Tests	54.051	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Ethanol	KIT 120 Tests	54.100	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Formalin	KIT 120 Tests	54.101	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANA HEp-2	IFA	S51.100	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® EMA	IFA	S512.050	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® EMA	IFA	S512.100	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® rLKS wrapped	IFA	S517.050	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® rLKS separated	IFA	S517.051	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® rLKS separated	IFA	S517.100	12-10-90-90-00	DE/CA33/9001/107/2

Product	Test	REF	EDMA	Registration Code
AESKUSLIDES® rLKS wrapped	IFA	S517.101	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® mLKS separated	IFA	S518.050	12-10-90-90-00	DE/CA33/9001/108/2
AESKUSLIDES® mLKS separated	IFA	S518.100	12-10-90-90-00	DE/CA33/9001/108/2
AESKUSLIDES® nDNA (Crithidia luciliae)	IFA	S53.100	12-10-01-05-00	DE/CA33/9001/105/1
AESKUSLIDES® ANCA Ethanol	IFA	S54.050	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Formalin	IFA	S54.051	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Ethanol	IFA	S54.100	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® ANCA Formalin	IFA	S54.101	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® CONJUGATE ANA HEp-2	IFA	C51.100	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® CONJUGATE ANA HEp-2 Bulk	IFA	C51.100.Bulk	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® CONJUGATE ANA HEp-2	IFA	C51.101	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® CONJUGATE ANA HEp-2 Bulk	IFA	C51.101.Bulk	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® CONJUGATE EMA IgA	IFA	C512.050	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® CONJUGATE EMA IgG	IFA	C512.060	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® CONJUGATE nDNA	IFA	C53.100	12-10-01-05-00	DE/CA33/9001/105/1
AESKUSLIDES® CONJUGATE ANCA Ethanol	IFA	C54.050	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® CONJUGATE ANCA Formalin	IFA	C54.051	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® CONJUGATE ANCA Ethanol	IFA	C54.100	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® CONJUGATE ANCA Formalin	IFA	C54.101	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® CONJUGATE LKS	IFA	CDTIFA	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® CONJUGATE LKS	IFA	CDTIFA.5	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® ANCA NEGATIVE CONTROL	IFA	NCANCA	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® IFA NEGATIVE CONTROL	IFA	NCIFA	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® ANA PATTERN CONTROL (Homogeneous)	IFA	PC51.100	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® ANA PATTERN CONTROL (Homogeneous)	IFA	PC51.101	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® EMA POSITIVE CONTROL IgA	IFA	PC512.050	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® EMA POSITIVE CONTROL IgG	IFA	PC512.060	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® AMA positive control 0,5 mL	IFA	PC517.050	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® nDNA POSITIVE CONTROL	IFA	PC53.100	12-10-01-05-00	DE/CA33/9001/105/1
AESKUSLIDES® C-ANCA PATTERN CONTROL	IFA	PC54.100	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® P-ANCA PATTERN CONTROL	IFA	PC54.101	12-10-90-90-00	DE/CA33/AES/2011/1/1
AESKUSLIDES® AMA POSITIVE CONTROL	IFA	PCDTIFA	12-10-90-90-00	DE/CA33/9001/107/2
AESKUSLIDES® COUNTERSTAIN (Evans Blue 0.2%)	IFA	EBIFA	12-10-90-16-00	DE/CA33/9001/109/1
AESKUSLIDES® MOUNTING MEDIUM	IFA	MMIFA	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® MOUNTING MEDIUM Bulk	IFA	MMIFA.Bulk	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® SAMPLE BUFFER	IFA	SBIFA	12-10-01-01-00	DE/CA33/9001/104/1
AESKUSLIDES® WASH BUFFER	IFA	WBIFA	12-10-01-01-00	DE/CA33/9001/104/1

AESKU.DIAGNOSTICS

Product	Test	REF	EDMA	Registration Code
AESQC®				
AESQC® Pool 1	MULTIPARAMETRIC CONTROLS	AESQCP1	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® Pool 2	MULTIPARAMETRIC CONTROLS	AESQCP2	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® Pool 3	MULTIPARAMETRIC CONTROLS	AESQCP3	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® Pool 4	MULTIPARAMETRIC CONTROLS	AESQCP4	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® Pool 5	MULTIPARAMETRIC CONTROLS	AESQCP5	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® Pool 6	MULTIPARAMETRIC CONTROLS	AESQCP6	15-50-01-01-00	DE/CA33/AES/2016/2
AESQC® Pool 7	MULTIPARAMETRIC CONTROLS	AESQCP7	15-50-01-01-00	DE/CA33/AES/2016/3
AESQC® Pool Mix	MULTIPARAMETRIC CONTROLS	AESQCPM	12-50-01-14-00	DE/CA33/AES/2009/1
AESQC® IFA Negative Control	MULTIPARAMETRIC CONTROLS	AESQCIFANEG	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Homogeneous	MULTIPARAMETRIC CONTROLS	AESQCANA01	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Centromere	MULTIPARAMETRIC CONTROLS	AESQCANA03	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Speckled	MULTIPARAMETRIC CONTROLS	AESQCANA04	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Nucleolar	MULTIPARAMETRIC CONTROLS	AESQCANA09	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Cytoplasmic	MULTIPARAMETRIC CONTROLS	AESQCANA21	12-50-01-14-00	DE/CA33/AES/2019/1
AESQC® ANA HEp-2 Panel 1	MULTIPARAMETRIC CONTROLS	AESQCIFANAP1	12-50-01-14-00	DE/CA33/AES/2019/1
SOFTWARE				
HERA	DATA MANAGEMENT SOFTWARE	HER-1000	27-02	DE/CA72/MZ/17/2019

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Wendelsheim, 2021-12-01

.....

Ort, Datum / place, date

.....

Dr. Torsten Matthias
CEO
Aesku.Diagnostics GmbH & Co. KG

CE

Declaration of Conformity

EUROIMMUN Medizinische Labordiagnostika AG
Seekamp 31, 23560 Lübeck, Germany

declares under its sole responsibility as manufacturer that the ELISA product

Anti-LC-1 ELISA (IgG) *EA 1307-9601 G*
(product name, order number)

meets the following demands of:

Directive 98/79/EC on in vitro diagnostic medical devices of 27 October 1998 and its transpositions in national laws which apply to it.

Conformity assessment procedure: Annex III

This Declaration of Conformity is valid based on the respective currently valid version of technical documentation.

Lübeck, May 19 2022
(Place and date of issue)

ppa
Dr. Ewald Müller-Kunert
- Head of Quality Management -

Susanne Aleksandrowicz
- Member of the Executive Board -

Anti-LC-1 ELISA (IgG)
Test instruction

ORDER NO.	ANTIBODIES AGAINST	IG CLASS	SUBSTRATE	FORMAT
EA 1307-9601 G	LC-1	IgG	Ag-coated microplate wells	96 x 01 (96)

Indications: The ELISA test kit provides a semiquantitative in vitro assay for human autoantibodies of the IgG class against liver cytosol antigen type 1 (LC-1) in serum or plasma for the diagnosis of increase in transaminases for unclear reasons and suspected autoimmune hepatitis.

Application: The determination of autoantibodies against LC-1 is another important supplementing serological parameter in the diagnosis of autoimmune liver diseases. A reliable diagnosis of AIH is indispensable since untreated AIH rapidly turns into liver cirrhosis.

Principle of the test: The test kit contains microplate strips, each with 8 break-off reagent wells coated with LC-1. In the first reaction step, diluted patient samples are incubated in the wells. If samples are positive, specific IgG antibodies (also IgA and IgM) bind to the antigens. To detect the bound antibodies, a second incubation is carried out using an enzyme-labelled anti-human IgG (enzyme conjugate) catalysing a colour reaction.

Contents of the test kit:

Component	Colour	Format	Symbol
1. Microplate wells coated with antigens 12 microplate strips each containing 8 individual break-off wells in a frame, ready for use	---	12 x 8	STRIPS
2. Calibrator (IgG, human), ready for use	dark red	1 x 2.0 ml	CAL
3. Positive control (IgG, human), ready for use	blue	1 x 2.0 ml	POS CONTROL
4. Negative control (IgG, human), ready for use	green	1 x 2.0 ml	NEG CONTROL
5. Enzyme conjugate peroxidase-labelled anti-human IgG (rabbit), ready for use	green	1 x 12 ml	CONJUGATE
6. Sample buffer ready for use	light blue	1 x 100 ml	SAMPLE BUFFER
7. Wash buffer 10x concentrate	colourless	1 x 100 ml	WASH BUFFER 10x
8. Chromogen/substrate solution TMB/H_2O_2, ready for use	colourless	1 x 12 ml	SUBSTRATE
9. Stop solution 0.5 M sulphuric acid, ready for use	colourless	1 x 12 ml	STOP SOLUTION
10. Test instruction	---	1 booklet	
11. Quality control certificate	---	1 protocol	

LOT Lot description
IVD In vitro diagnostic medical device
CE
Storage temperature
Unopened usable until

Storage and stability: The test kit has to be stored at a temperature between +2°C to +8°C. Do not freeze. Unopened, all test kit components are stable until the indicated expiry date.

Waste disposal: Patient samples, calibrators, controls and incubated microplate strips should be handled as infectious waste. All reagents must be disposed of in accordance with local disposal regulations.

Preparation and stability of the reagents

Note: All reagents must be brought to room temperature (+18°C to +25°C) approx. 30 minutes before use. After first use, the reagents are stable until the indicated expiry date if stored at +2°C to +8°C and protected from contamination, unless stated otherwise below.

- **Coated wells:** Ready for use. Tear open the resealable protective wrapping of the microplate at the recesses above the grip seam. Do not open until the microplate has reached room temperature to prevent the individual strips from moistening. Immediately replace the remaining wells of a partly used microplate in the protective wrapping and tightly seal with the integrated grip seam (Do not remove the desiccant bag).
  Once the protective wrapping has been opened for the first time, the wells coated with antigens can be stored in a dry place and at a temperature between +2°C and +8°C for 4 months.

- **Calibrator and controls:** Ready for use. The reagents must be mixed thoroughly before use.

- **Enzyme conjugate:** Ready for use. The enzyme conjugate must be mixed thoroughly before use.

- **Sample buffer:** Ready for use.

- **Wash buffer:** The wash buffer is a 10x concentrate. If crystallisation occurs in the concentrated buffer, warm it to +37°C and mix well before diluting. The quantity required should be removed from the bottle using a clean pipette and diluted with deionised or distilled water (1 part reagent plus 9 parts distilled water).
  For example: For 1 microplate strip, 5 ml concentrate plus 45 ml water.
  The working strength wash buffer is stable for 4 weeks when stored at +2°C to +8°C and handled properly.

- **Chromogen/substrate solution:** Ready for use. Close the bottle immediately after use, as the contents are sensitive to light ✳. The chromogen/substrate solution must be clear on use. Do not use the solution if it is blue coloured.

- **Stop solution:** Ready for use.

Warning: The calibrator and controls of human origin have tested negative for HBsAg, anti-HCV, anti-HIV-1 and anti-HIV-2. Nonetheless, all materials should be treated as being a potential infection hazard and should be handled with care. Some of the reagents contain the agent sodium azide in a non-declarable concentration. Avoid skin contact.

Preparation and stability of the patient samples

Samples: Human serum or EDTA, heparin or citrate plasma.

Stability: Patient samples to be investigated can generally be stored at +2°C to +8°C for up to 14 days. Diluted samples should be incubated within one working day.

Sample dilution: Patient samples are diluted **1:101** in sample buffer. For example: dilute 10 µl sample in 1.0 ml sample buffer and mix well by vortexing (sample pipettes are not suitable for mixing).

NOTE: The calibrator and controls are prediluted and ready for use, do not dilute them.

Incubation

Sample incubation: (1st step)
Transfer 100 µl of the calibrator, positive or negative control or diluted patient samples into the individual microplate wells according to the pipetting protocol. Incubate for **30 minutes** at room temperature (+18°C to +25°C).

Washing:
Manual: Empty the wells and subsequently wash 3 times using 300 µl of working strength wash buffer for each wash.
Automatic: Wash the reagent wells 3 times with 450 µl of working strength wash buffer (program setting: e.g. TECAN Columbus Washer "Overflow Mode").

Leave the wash buffer in each well for 30 to 60 seconds per washing cycle, then empty the wells. After washing (manual and automated tests), thoroughly dispose of all liquid from the microplate by tapping it on absorbent paper with the openings facing downwards to remove all residual wash buffer.

Note: Residual liquid (> 10 µl) remaining in the reagent wells after washing can interfere with the substrate and lead to false low extinction values. Insufficient washing (e.g., less than 3 wash cycles, too small wash buffer volumes, or too short residence times) can lead to false high extinction values.
Free positions on the microplate strip should be filled with blank wells of the same plate format as that of the parameter to be investigated.

Conjugate incubation: (2nd step)
Pipette 100 µl of enzyme conjugate (peroxidase-labelled anti-human IgG) into each of the microplate wells. Incubate for **30 minutes** at room temperature (+18°C to +25°C).

Washing:
Empty the wells. Wash as described above.

Substrate incubation: (3rd step)
Pipette 100 µl of chromogen/substrate solution into each of the microplate wells. Incubate for **15 minutes** at room temperature (+18°C to +25°C) protect from direct sunlight.

Stopping:
Pipette 100 µl of stop solution into each of the microplate wells in the same order and at the same speed as the chromogen/substrate solution was introduced.

Measurement:
Photometric measurement of the colour intensity should be made at a wavelength of 450 nm and a reference wavelength between 620 nm and 650 nm **within 30 minutes of adding the stop solution**. Prior to measuring, slightly shake the microplate to ensure a homogeneous distribution of the solution.

Pipetting protocol

	1	2	3	4	5	6	7	8	9	10	11	12
A	**C**	**P 6**	**P 14**	**P 22**								
B	**pos.**	**P 7**	**P 15**	**P 23**								
C	**neg.**	**P 8**	**P 16**	**P 24**								
D	**P 1**	**P 9**	**P 17**									
E	**P 2**	**P 10**	**P 18**									
F	**P 3**	**P 11**	**P 19**									
G	**P 4**	**P 12**	**P 20**									
H	**P 5**	**P 13**	**P 21**									

The above pipetting protocol is an example of the semiquantitative determination of antibodies in 24 patient samples (P 1 to P 24).

Calibrator (C), positive (pos.) and negative (neg.) control as well as the patient samples have been incubated in one well each. The reliability of the ELISA test can be improved by duplicate determinations of each sample.
The wells can be broken off individually from the strips. This makes it possible to adjust the number of test substrates used to the number of samples to be examined and minimises reagent wastage.
Both positive and negative controls serve as internal controls for the reliability of the test procedure. They should be assayed with each test run.

Calculation of results

Semiquantitative: Results can be evaluated semiquantitatively by calculating a ratio of the extinction value of the control or patient sample over the extinction value of calibrator. Use the following formula to calculate the ratio:

$$\frac{\textbf{Extinction of the control or patient sample}}{\textbf{Extinction of calibrator}} = \textbf{Ratio}$$

EUROIMMUN recommends interpreting results as follows:

Ratio <1.0: **negative**
Ratio ≥1.0: **positive**

For duplicate determinations the mean of the two values should be taken. If the two values deviate substantially from one another, EUROIMMUN recommends retesting the samples.

For diagnosis, the clinical picture of the patient patient always needs to be taken into account along with the serological findings.

Test characteristics

Calibration: As no international reference serum exists for antibodies against LC-1, the results are given as a ratio. This represents a relative measurement for the concentration of antibodies in serum or plasma.

For every group of tests performed, the extinction values of the calibrator and the ratio of the positive and negative control sera must lie within the limits stated for the relevant test kit lot. A quality control certificate containing these reference values is included. If the values specified for the control sera are not achieved, the test results may be inaccurate and the test should be repeated.

The binding activity of the antibodies and the activity of the enzyme used are temperature-dependent. It is therefore recommended using a thermostat in all three incubation steps. The higher the room temperature (+18°C to +25°C) during the incubation steps, the greater the extinction values will be. Corresponding variations apply also to the incubation times. However, the calibrator is subject to the same influences, so that such variations will be largely compensated in the calculation of the result.

Antigen: The microplate wells were coated with recombinant LC-1. The corresponding human cDNA was expressed in insect cells using a baculovirus vector. The specific target antigen of anti-LC-1 antibodies was identified in 1999 as the enzyme formiminotransferase cyclodeaminase (Lapierre et al.).

Detection limit: The lower detection limit is defined as the mean value of an analyte-free sample plus three times the standard deviation and is the smallest detectable antibody titer. The lower detection limit of the Anti-LC-1 ELISA (IgG) is ratio 0.05.

Cross reactivity: This ELISA specifically detects autoantibodies of class IgG against LC-1. When investigating patient sera for autoantibodies against SLA (n = 2) and LKM (n = 8) no cross reactions were found.

Interference: Haemolytic, lipaemic and icteric samples showed no influence on the result up to a concentration of 10 mg/ml for haemoglobin, 20 mg/ml for triglycerides and 0.4 mg/ml for bilirubin in this ELISA.

Reproducibility: The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation (CV) using 3 samples. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on 4 determinations performed in 6 different test runs.

Intra-assay variation, n = 20		
Sample	**Mean value (Ratio)**	**CV (%)**
1	3.1	4.9
2	4.7	2.7
3	8.0	2.4

Inter-assay variation, n = 4 x 6		
Sample	**Mean value (Ratio)**	**CV (%)**
1	2.5	10.8
2	3.8	10.2
3	6.7	9.4

Prevalence and specificity: Sera of 93 patients with autoimmune hepatitis, 183 patients with hepatitis A, hepatitis B, toxic liver diseases, steatohepatitis or primary biliary cirrhosis (PBC) and 200 healthy blood donors were examined with the EUROIMMUN Anti-LC-1 ELISA (IgG). The prevalence of antibodies against LC-1 in autoimmune hepatitis was 5.4% with a specificity of 100%.

Reference range: The levels of the anti-LC-1 antibodies (IgG) were analysed with this EUROIMMUN ELISA in a panel of 200 healthy blood donors. With a cut-off ratio of 1.0, all blood donors were anti-LC-1 negative.

Literature references

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